BIOINFORMATION
Discovery at the interface of physical and biological sciences

OPEN ACCESS GOLD

BIOMEDICAL INFORMATICS

www.bioinformation.net
Volume 17(5)

Research Article

Molecular docking analysis of potential compounds from an Indian medicinal soup "kabasura kudineer" extract with IL-6

S. Saleem Basha[1], Dhirendra Tripathi[2], Sravanthi Koora[3], K. Satyanarayana[4*] & Selvaraj Jayaraman[5]

[1]Dept of Medical Biochemistry, School of Medicine, Haramaya University, Harar Campus, Ethiopia; [2]Department of Otorhinolaryngology, Government Medical College, Shivpuri, Shivpuri- 473638; [3]Department of Pharmacology, Government Medical College Siddipet-502103, Siddipet, Telangana; [4]Department of Biochemistry, Government Medical College Siddipet, Siddipet 502103 Telangana India; [5]Department of Biochemistry, Saveetha Dental College and Hospitals, Saveetha Institute of Medical and Technical Sciences, Chennai-600 077, India, Dr. K.Satyanarayana - Email ID: satya79700@gmail.com Corresponding author*

Received April 25, 2021; Revised May 27, 2021; Accepted May 28, 2021, Published May 31, 2021

DOI: 10.6026/97320630017568

Declaration on official E-mail:
The corresponding author declares that official e-mail from their institution is not available for all authors

Declaration on Publication Ethics:
The authors state that they adhere with COPE guidelines on publishing ethics as described elsewhere at https://publicationethics.org/. The authors also undertake that they are not associated with any other third party (governmental or non-governmental agencies) linking with any form of unethical issues connecting to this publication. The authors also declare that they are not withholding any information that is misleading to the publisher in regard to this article.

Abstract:
The use of "kabasura kudineer" (liquid soup made from Indian medicinal plants) for combating COVID-19 has been common in the states of Tamilnadu and Puducherry, India during the pandemic. Therefore, it is of interest to document the molecular docking analysis of IL-6 inhibitors with potential antiviral compounds from "kabasura kudineer" extract. We show the optimal binding features of gallic acid and luteolin with the Interleukin-6 protein for further consideration.

Key words: Molecular docking, IL-6, CoVid-19, "kabasura kudineer"

Background:
Symptoms of the novel corona virus are similar to normal flu linked to CoVid-19 in structure and cause **[1-8].** Jing Liu *et al.* **[7]** reported that CoVid-19 patients sustained decrease in the proportion of lymphocytes with increase in the inflammatory cytokines (interleukin) in the peripheral blood. It is also known that IL-6 binds with gp130 to initiate downstream signal transduction, gene expression, and intracellular signal transduction **[9-20].** The design, development and evaluation of compounds to combat the viral pandemic are gaining momentum. The use of "kabasura kudineer" (liquid soup from Indian medicinal plants) for combating CoVid-19 has been common in the states of Tamilnadu and Puducherry during the pandemic. Therefore, it is of interest to

BIOINFORMATION
Discovery at the interface of physical and biological sciences

document the molecular docking analysis of compounds from an Indian medicinal soup "kabasura kudineer" extract with IL-6.

Material and Methods:

Molecular docking analysis was performed using the Maestro 11.4, Schrodinger 2017-4 **[21-22].**

Ligand preparation:

38 reported antiviral compounds **[23-26]** were used as ligands for the molecular docking analysis. PubChem and Drug Bank were used to download the 2D structures for the ligands. LigPrep module (Schrodinger, LLC, NY, USA, 2009) was utilized from the Maestro developer to design and create the 3D ligand structures by eliminating salt, adding hydrogen molecules, and ionizing at pH (7.0 +/- 2.0). Energy minimization was performed utilizing OPLS3 force field by utilizing the standard energy capacity of atomic mechanics. A RMSD cut-off at 0.01 Å was used to create the low-energy ligand isomer.

Preparation of protein structures

Protein structure of IL-6 (PDB IDs: 3L5I, having resolution < 1.90 , R-value free <0.222, R-Value Work <0.181) was downloaded from the Protein Data Bank (http://www.rscb.org) **[27].** Assigned bonds orders and hydrogen atoms were added. Water molecules were removed within 3 of HET groups **[20].** OPLS3 force field in Schrodinger, LLC, NY, USA, 2009 was used for energy minimization **[28].** The receptor grid boxes were generated using Glide's Receptor Grid Generation module at the active site (with the radius of 20 around the crystal structure) of co-crystallized ligand with the computing cubic box of 14.74 × 53.85 × 73.53 .

Molecular docking

Flexible docking with GLIDE Extra precision (XP) convention was used for calculating the binding affinity and ligand efficiency as an inhibitor of Corona virus target **[29-30].** Maestro interface (Schrodinger Suite, LLC, NY) was used as the visualization tool for docked ligands**.**

Table 1: List of antiviral compounds in the composition of Kabasura (cold fever) Kudineer (concoction – mixture of ingredients) Chooranam (powder)

Plant Name	Compound name
Zingiber officinale rosc	β-sesquiphellandrene
	β-bisabolene
	Geranial
Piperlongum L	Piperine
	Piperlonguminine
Syzygium aromaticum	Eugenol
	b-Caryophyllene
Tragia involucrata L	Stigmosterol
	3-(2,4-dimethoxyphenyl)-6,7-dimethoxy-2, 3-dihydrochromen-4-one
Anacyclus pyrethrum	Squalene
	γ-Sitosterol
Andrographi spaniculata	Andrograpanin
	5-Hydroxy-7, 8-dimethoxyflavanone
Hygrophilla auriculata (Schum.) Heine	Lupeol
	Betulin
Terminalia chebula Retz.	Chebulagicacid
	Gallicacid
Justicia adhatoda L.	Vasicinone
	Carvacrol
Plectranthus amboinicus (Lour) Spreng	Cirsimaritin
	Chrysoeriol
	6-Methoxygenkwanin
Costus speciosus	Luteolin
	Costunolide
	Elemol
Tinospora cordifolia (wild)	Tinosponone
Miers Ex Hook f & Thomas	Bharangin
Clerodendrum serratum L.	Scutellarein
	Magnoflorine
Sida acuta Burm f	Cycleanine
	Cyperene
Cypreus rotundus L.	beta-selinene

BIOINFORMATION
Discovery at the interface of physical and biological sciences

JACOM Formulation	
Justicia adathoda L.	Vasicine
Carica papaya	Quercetin
Andrographis paniculata Burm. f. Nees	Andrographolide
Ocimum tenuiflorum	Ursolicacid
Standard antiviral compound	Hydroxychloroquine
	Abacavir

Table 2: Comparison of binding features for top two compounds with 2 standard anti-viral compounds against IL-6.

Compound Name	Compound Id	Docking score	Xp GScore	Hydrogen Bonds Interaction	Other Interaction
Gallic acid	CID_370	-6.826	-6.826	VAL477, TRY478, ALA479	LYS430 (Salt Bridge)
Luteolin	CID_5280445	-6.604	-6.621	LYS429, THR393, TYR478, and ALA479	LYS430 (pi-cation interaction)
Hydroxychloroquine	CID_ 3652	-6.239	-6.289	ASP452	ASP452
Abacavir	CID_441300	-5.053	-5.058	TRY478, THR393, ALA389, VAL391	-

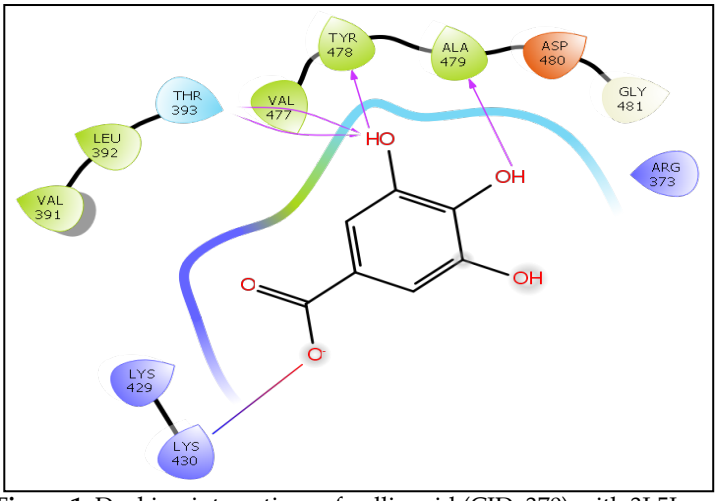


Figure 1: Docking interactions of gallic acid (CID_370) with 3L5I.

Results and Discussion:

The use of "kabasura kudineer" (liquid soup from Indian medicinal plants) for combating COVID-19 has been common in the states of Tamilnadu and Puducherry during the pandemic. Therefore, it is of interest to document the molecular docking analysis of IL-6 inhibitors with potential antiviral compounds from "kabasura kudineer" extract (**Table 1**). The potential binding residues in IL-6 are TYR, ALA, VAL, LYS, TRY, THR, and ASP. 38 molecules were docked with IL-6 and ranked based on their dock score. Compounds with optimal binding features are given in **Table 2**. **Table 2** shows that compounds (gallic acid and luteolin) showed good binding interactions with IL-6 structures compared to known standard compounds. Compound 1 (gallic acid) has one salt bridge interaction with LYS430 and three hydrogen bonding interactions with VAL477, TRY478, and ALA79 **(Figure 1).** It also has more lipophilic interactions and non-bonded interactions against IL-6. When comparing to other compounds including the standard anti-HIV drugs, gallic acid has a more binding affinity towards IL-6 and it showed best hydrogen bonding interactions. Compound 2 (luteolin) has one pi-stacking interaction with LYS430 and four hydrogen-bonding interactions with LYS429, THR393, TYR478, and ALA479 **(Figure 2).** It also has more lipophilic interactions and non-bonded interactions against IL-6. When comparing to other compounds including standard anti-HIV drugs, Luteolin has good binding affinity, hydrogen bond towards IL-6. Thus, data show that they are involved in non-bonded interaction with IL-6.

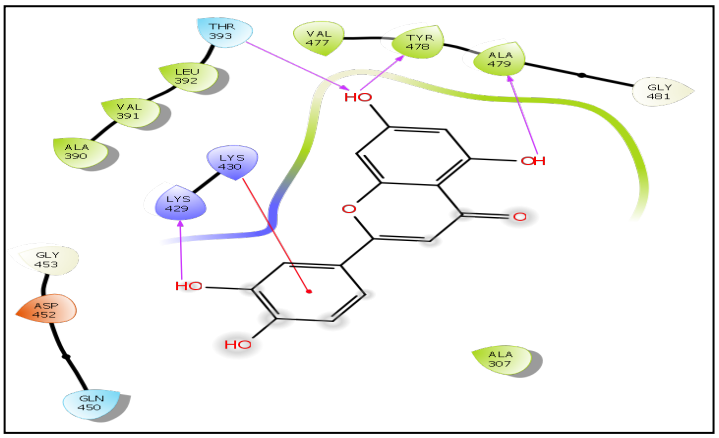


Figure 2: Docking interactions of luteolin (CID_5280445) with 3L5I.

Conclusion:

We report that gallic acid and luteolin have good binding features with the Interleukin-6 protein for further consideration. Thus, kabasura kuduneer extract containing gallic acid and luteolin used in combating COVID-19 is of importance.

BIOINFORMATION
Discovery at the interface of physical and biological sciences

Conflict of Interest: None declared.

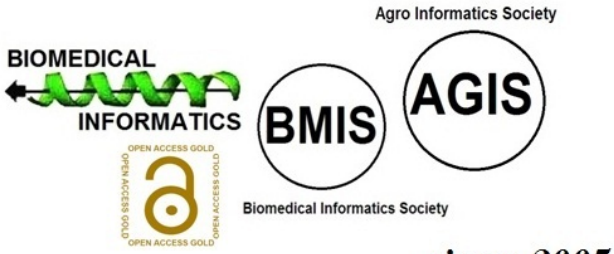
References:

[1] Van der Hoek. L *et al. Nat Med.* 2004 **10**:368. [PMID: 15034574].
[2] Sohrabi C *et al. Int J Surg.* 2020 **76:**71. [PMID: 32112977].
[3] *von* Tigerstrom BJ *et al. J Travel Med.* 2020 **27(8):** 127. [PMID: 32749458]
[4] Perlman S *et al. Nat Rev Microbiol.* 2009 **7:** 439-50. [PMID: 19430490].
[5] Lu, R *et al. Lancet* 2020 **395**: 565. [PMID: 32007145].
[6] Jing Liu *et al. Bio Medicine* 2020 **55**:102763. [PMID: 32361250].
[7] Yin Y *et al. Respirology.* 2018 **23**:130. [PMID: 29052924].
[8] Rose-John S. *Int J Biol Sci.* 2012 8:1237. [23136552].
[9] Kurzrock R *et al. Cancer Res.* 1993 **53**:2118. [PMID: 8481913]
[10] Seymour JF *et al. Am J Med.* 1997 **102:** 21. [PMID: 9209197]
[11] Ebrahimi B et al. *Cancer.* 2004 **101:**2727. [PMID: 15526319].
[12] Johnson DE *et al. Nat Rev Clin Oncol.* 2018 **15:**234. [PMID: 29405201].
[13] Villarino AV, *et al. Nat Immunol.* 2017 **18:**374. [PMID: 28323260].
[14] Zegeye MM *et al. Cell Commun Signal.* 2018 **16:**55. [PMID: 30185178].
[15] Su H *et al. Front Immunol.* 2017 **8:** 405. [PMID: 28484449].
[16] Heinrich PC *et al. Biochem J.* 2003 **374:**1. [PMID: 12773095].
[17] Taniguchi K *et al. Nature.* 2015 **519:**57. [PMID: 25731159].
[18] Yamada O *et al. Mol Cancer Ther.* 2012 **11:**1112. [PMID: 22402124].
[19] Hiem S *et al. J Clin Invest.* 2013 **123:**767. [PMID: 23321674]
[20] Cheeseright T *et al. J Chem Inf Model.* 2006 **46:**665. [PMID: 16562997].
[21] Bauer MR & Mackey MD. *J Med Chem.* 2019 **62:**3036. [PMID: 30807144].
[22] Siddha formulary of India Part II. Delhi: The controller of Publications; **2011** p.160-192.
[23] Denyer CV, *et al. J Nat Prod.* 1994 **57:**658. [PMID: 8064299].
[24] Koch C *et al. Phytomedicine.* 2008 **15:**71. [PMID: 17976968].
[25] Jiang ZY, *et al. Bioorg Med Chem Lett.* 2013 **23:**2123. [PMID: 23434420].
[26] Xu Y, *et al. J Biol Chem.* 2010 **285:**21214. [PMID: 20489211].
[27] Halgren TA, *et al. J Med Chem.* 2004 **47:**1750. [PMID: 15027866].
[28] Carlesso A, *et al. Sci Rep.* 2019 **9:**3407. [PMID: 30833722].
[29] Huang H, *et al. Front Chem.* 2018 **6:**138. [PMID: 29868550].
[30] Shah B *et al. Life Sci.* 2020 **252:**117652. [PMID: 32278693].

Edited by P Kangueane
Citation: Saleem Basha ***et al.*** Bioinformation 17(5): 568-572 (2021)

BIOINFORMATION
Discovery at the interface of physical and biological sciences

OPEN ACCESS GOLD



since 2005

BIOINFORMATION
Discovery at the interface of physical and biological sciences

indexed in