Study of antiviral activity of the genus *Ocimum* against COVID-19 through *in silico* method

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Abstract
Ocimum is one of the largest genus under the Lamiaceae family, with over 150 aromatic species, used as source of essential oils. Essential oils and extracts present in the genus Ocimum have antiviral properties. Corona virus disease 2019 (COVID-19) is an infectious disease caused by SARS-CoV-2, a pathogenic Corona virus that causes respiratory illness in human body and has now emerged as a serious global concern. Despite the fact that multiple vaccines for Covid-19 have been authorised to date, lead compounds are still in great demand in order to produce more promising or effective medicines and vaccines.

The current study is an attempt to screen a total 11 antiviral aroma compounds obtained from Ocimum species, employed as ligand molecules, with Remdesivir serving as the reference medication. The chosen ligands were docked with the two primary therapeutic targets of SARS-CoV-2, Proteases 3CLpro and Spike Glycoprotein. ADMET features of the screened compounds were evaluated. Docking findings found that rosmarinic acid and apigenine have strong Moldock scores with each target, similar to the current COVID-19 drug Remdesivir. Docking and ADMET experiments show that rosmarinic acid and apigenine are potentially effective lead compounds for the treatment of COVID-19.

Keywords: *Ocimum*, Essential oils, Antiviral, COVID-19, Molecular docking, ADMET.

Introduction

Severe acute respiratory syndrome coronavirus-CoV2 belongs to the Orthocoronavirinae subfamily and is the cause of the COVID-19 disease [1]. The disease first appeared in the Chinese city city Wuhan in the month of December 2019. On March 11, 2020, the disease was declared as Pandemic by the World Health Organization and has become a big challenge in the history of medical science. Although different vaccines have been discovered, no vaccine that is truly effective, has been discovered. Till date a number of vaccines were developed which are: Pfizer, Moderna, Janssen, AstraZeneca, Novavax etc. but all of them have some or more conditions regarding their effectiveness. For example, Pfizer is approved for the people, who are above twelve year of age whereas Moderna is approved for above the age 18 years. Some of them have side effects such as fatigue, headache, muscle pain etc.[21]

Despite the fact that several medications have been explored for COVID-19, none of them have been authorised. All coronavirus enzymes and proteins involved in viral replication and the manipulation of host cellular processes are potential drug targets in the search for SARS-CoV-2 treatment solutions.

Spike's (S) Glycoprotein in CoVs mediates virus entrance by interacting with specific host-receptors on the cell's surface, making it an intriguing therapeutic target[30]. Wrapp et al[35] crystallised SARS-CoV-2 spike glycoprotein and renamed it 6VSB in the Protein Data Bank[8]. Proteases 3CLpro (3C-like protease or main protease) are essential for virus replication and modulating the host cell response, making them prime candidates for antiviral medication development[15,28]. Liu et al[20] solved the crystal structure of COVID-19's primary protease protein (PDB code: 6LU7)[3]. We chose these two essential SARS-CoV-2 proteins as therapeutic targets.

A number of medicinal plants have shown promise in treating a variety of viral diseases, with some exhibiting broad-spectrum antiviral action[23]. Among the plants with antiviral capability are some species of the genus *Ocimum*, which belongs to the family Lamiaceae. It is the largest genus of Lamiaceae family, with more than 150 species and are regarded as source of essential oils (EO). Some of the mostly cultivated species are *Ocimum gratissimum* L., *O. basilicum* L., *O. tenuiflorum* L., *O. africanum* Lour., *O. americanum* Lour., *O. minimum* L. and *O. canum* Sims[24, 33]. Several investigations have been done and extracted a large number of EO components and extracts from various *Ocimum* species (Table 1).

The proliferation of viruses can be restricted by essential oils. Compounds such as methyl chavicol, trans-anethole, eugenol, methyl-eugenol, β-eudesmol, farnesol, β-caryophyllene and β-caryophyllene oxide, γ-terpinene, 4-allylanisole, dihydrocarvone, D-limonene, cuminyl aldehyde, cuminol, camphor, camphene, isoborneol, L-bornyl acetate, 2-decanol, 2-heptanol, methylheptane, nerol, isopulegol and citral are present in the EO of some species of *Ocimum*.

However, only a few of these compounds have been documented to be effective against viruses such as HSV-1, HSV-2, parainfluenza type-3 (PI-3), hepatitis C virus

(HCV), enterovirus 71 (EV71), adenovirus (ADV), bovine herpes virus (BHV-1) and human rotavirus (RV) (as shown in table 1)[1,26]. Taking these points into account, we are attempting to assess the antiviral activity of aroma compounds from some *Ocimum* species using an *in silico* technique.

Materials and Methods

Compound Selection and ligand preparation: We have chosen 11 aroma compounds from some *Ocimum* species as ligands based on their antiviral activity (Figure 1) and remdesivir as the reference medication. ChemDraw Ultra 12.0.2.1076 (Cambridge Soft) was used for ligand preparation. The ligands' 2D structures were first sketched and then converted to 3D. ChemDraw 3D was used to optimize the three-dimensional structures of the selected and reference drug compounds, reducing their energy with a 0.1 RMS gradient for geometry optimization.

Protein preparation: Protein data bank was used to download the crystal structures of COVID-19 major protease (6LU7) and SARS-CoV-2 spike glycoprotein (PDB ID: 6VSB). The MVD protein preparation tab was activated to eliminate the associated ligand, water and co-factors. In automatic preparation mode, hybridization state, bond order and explicit hydrogens were assigned, along with charges based on the MolDock Scoring Function. The MVD grid-based cavity prediction algorithm was utilized to predict the protein's binding sites, with a grid resolution set to 0.8 to encompass the protein. The grid points' accessibility was assessed by placing spheres with a 1.4 radius for Van der Waals overlap analysis. Random directions were chosen from every accessible grid point to detect any inaccessible points encountered during the procedure. This procedure was iterated in 16 distinct directions and if 12 or more lines came across an inaccessible volume, the point was labeled as inaccessible.

Table 1
Phytochemicals present in different species of *Ocimum* with antiviral Activity

Species	Phytochemicals	Antiviral Activity against
Ocimum basilicum L.[3,6,18]	1,8-cineole ,Camphor, Thymo, Eugenol, Eugenol, Epoxide, Apigenine, Linaloo, Ursolic acid	HSV 1 et 2 (DNA enveloped virus), HIV -1 (RNA nonenveloped virus
O. sanctum L.[5]	Ursolic acid,Eugenol, 1,8-cineole. Rosmarinic acid	HSV-1,2
O. campechianum Mill.[2,39]	1,8-cineole. β-caryophyllen	HSV-1
O.gratissimum L.[4]	Eugenol, Thymol	HSV-1,2
O. americanum L.[7]	Rosmarinic acid, Oleanolic acid	HIV-1
O. citriodorum Lour.[2]	Caffeic acid, Linalool	HSV-1
O. kilimandscharicum Guerke.[2]	1,8-cineol, Terpinen-4-ol	HSV-1
O. micranthum Willd[35]	Ursolic acid	HSV-1
O. selloi Benth.[2]	Trans-Anethole	HSV-1,2

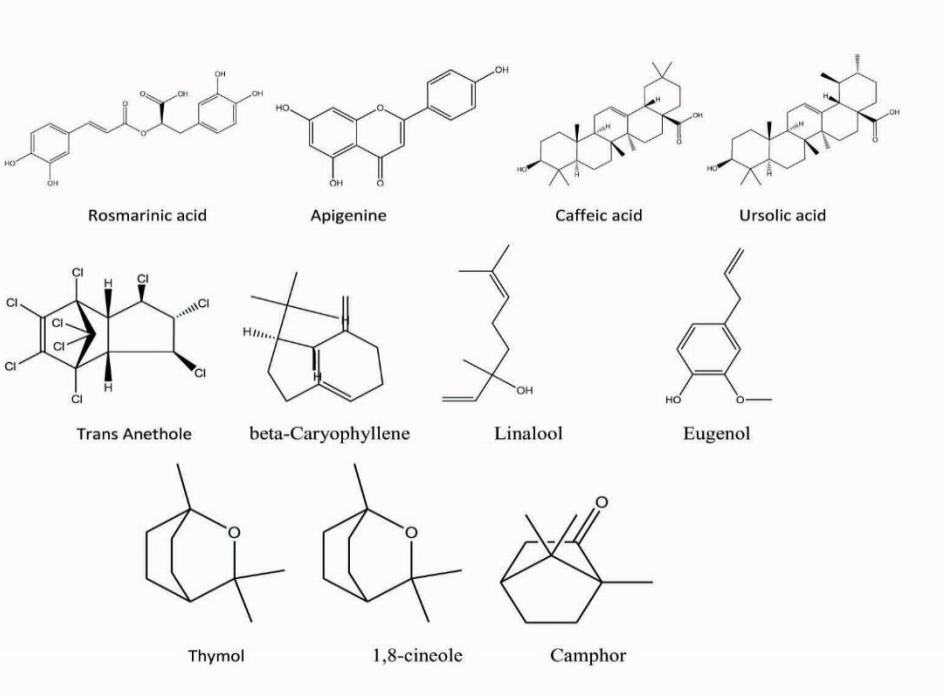

Figure 1: Selected aroma compounds from the genus *Ocimum*

After connecting the neighbouring grid points, volumes less than 10.0 3 were deleted as unimportant[29]. The predicted cavities were scored and ordered based on their volumes, with the highest scoring one being chosen. The volume of the 6LU7 cavity is 127.488 (Å3), the surface is 423.68 (Å2), the volume of the 6VSB cavity is 460.8 (Å3) and the surface is 1815.04(Å2).

Molecular docking: Molecular docking helps to assess a compound's ability to bind to a target protein[27]. Using Molegro virtual docker, the aroma compounds of *Ocimum* species and the reference medicine remdesivir were allowed to dock with the residues of the identified cavity of COVID -19 major protease and spike glycoprotein (trial version). The grid points were docked using MolDock Score (GRID) and their energy potential was evaluated using tri-linear interpolation. The scoring function MolDock SE (Simplex Evolution) was employed, with a maximum of 1500 iterations, a population size of 50 and conducted over 5 runs.

Upon the completion of docking, the top conformations involving both proteins were chosen for additional analysis using Moldock or docking scores, which is a statistical scoring method that assigns numerical values to interaction energy[9]. Two of the finest poses, as well as the Chloroquine remdesivir posture, were then converted to ligand and H-bond interactions between the ligand and the chosen targets were investigated.

ADME and toxicity prediction: The study involved the analysis of absorption, distribution and ADME properties including parameters for intestinal absorption obtained from *in vitro* models such as human colon adenocarcinoma (Caco-2) and Madin-Darby canine kidney cell (MDCK) to observe the human intestinal absorption percentage (HIA)26. Predictions were made regarding key pharmacokinetic properties such as Blood-Brain Barrier (BBB) permeability, Plasma Protein Binding (PPB) and CYP 3A4 metabolism of the 7 best ligands from docking results using preADMET.

Results and Discussion

Molecular docking: In this study, we have taken 11 *Ocimum* fragrance compounds as ligands, including the antiviral medication Remdesivir, to perform molecular docking with two essential SARS-CoV-2 proteins. The antiviral potential of selected ligands was assessed by analysing their post docking interactions and scores with two SARS-CoV-2 pharmacological targets. The MolDock score (kcal/mol) was used to evaluate the docking outcomes. Table 2 shows the docking findings for the selected ligands and two selected targets. Two fragrance compounds, rosmarinic acid and apigenine, exhibited good docking scores with both SARS-CoV-2 target proteins. Following that, the H-Bond interaction between the best ligand and each of the selected target proteins was examined.

H-Bond interaction: H-Bond interactions are weak and quickly disrupted, yet they play a key role in both protein-ligand interactions and the stability of ligand-protein interactions[12,20]. In this context, the best-performing ligands in each protein were chosen to examine H-Bond interactions with the relevant residues (Table 1). Rosmarinic acid and apigenine, two ligands, have demonstrated strong H-bond interaction with both target and reference medication Remdesivir (Figures 2-4). These H-bond interactions, along with the Moldock score, demonstrated their antiviral efficacy against SARS-COV-2.

ADME and toxicity study: In the process of discovering and developing pharmaceutical candidates, absorption, distribution, metabolism, excretion and toxicity (ADMET) are crucial properties.

In admetSAR1, we made predictions on various ADMET properties, such as Blood-Brain Barrier (BBB) penetration, Human Intestinal Absorption (HIA), Caco-2 Permeability (Caco-2), CYP metabolism, AMES toxicity and carcinogenicity, as depicted in table 4.

Table 2
Results of Molecular docking

COVID-19 main protease(6LU7)		**Spike (S) Glycoprotein (6VSV)**	
Ligand	**MolDock Score (kcal/mol)**	**Ligand**	**MolDock Score (kcal/mol)**
*remdesivir	-173.12	*remdesivir	-113.625
Rosmarinic acid	-130.68	Rosmarinic acid	-91.531
Apigenine	-116.93	Caffeic acid	-73.177
Caffeic acid	-102.79	Trans Anethole	-72.631
Ursolic acid	-98.255	Apigenine	-70.944
Trans Anethole	-82.558	Ursolic acid	-70.894
beta-Caryophyllene	-81.097	beta-Caryophyllene	-59.997
Linalool	-79.804	Linalool	-56.465
Eugenol	-73.102	Eugenol	-49.092
Thymo	-70.066	Thymo	-46.502
1,8-cineole	-60.754	Camphor	-35.991
Camphor	-54.099	1,8-cineole	-32.729

*reference drug

Table 3
Hydrogen bonding pattern at the binding sites of the targets

Compound	H-bond with COVID-19 main protease(6LU7)	H-bond with 3VSB Spike (S) Glycoprotein (6VSV)
*Remdesivir	O (Thr 26)-H-O O (Asn 142)-H-O O (Ser 144)-H-N O (Ser 144)-H-O N (Hos 163)-H-N N (Glu 166)-H-O	N (Asn 960)-H-O N (Lys 278)-H-O
Rosmarinic acid	N (His 41)-H-O O (Tyr 54)-H-O O (Glu 166)-H-O N (His 163)-H-O O (Thr 190)-H-O O (Phe 140)-H-O	O (Asn 960)-H-O N (Arg 44)-H-O N (His 49)-H-O O (Ser 50)-H-O
Apigenine	O (Gln 189)-H-O O (Asp 187)-H-O O (Thr 190)-H-O O (Gln 192)-H-O	O (Ser 50)-H-O O (Ser 50)-H-O N (Val 963)-H-O O (Leu 48)-H-O

*Drug compound

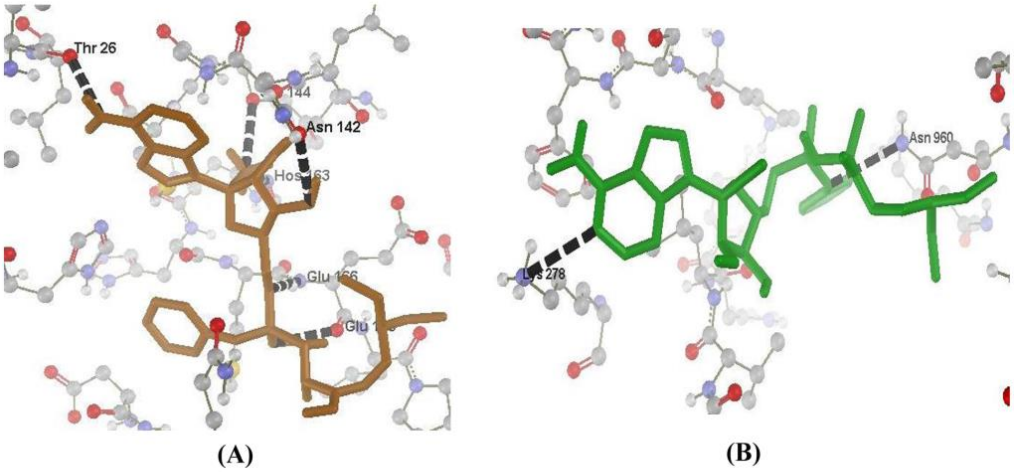

Figure 2: Residues interacting with remdesivir forming Hydrogen bonds (black dash lines) in (a) COVID-19 main protease protein; (b) spike glycoprotein of SARS-CoV-2.

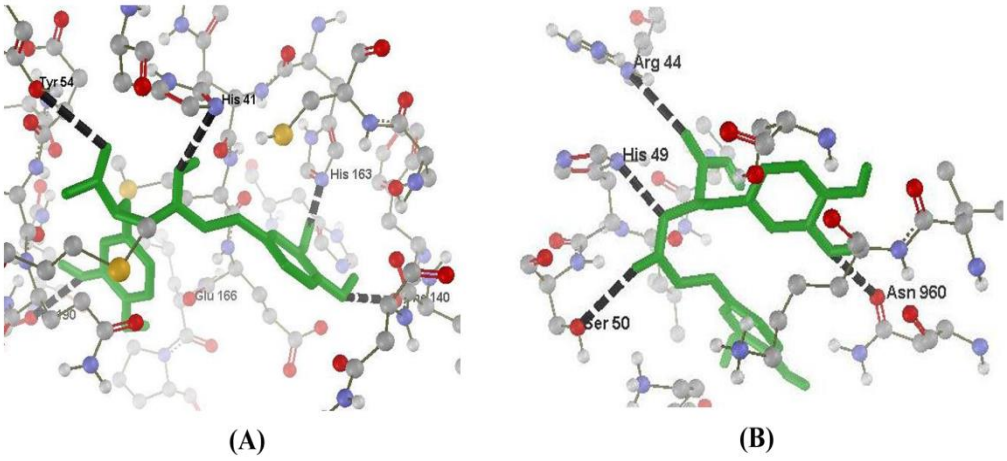

Figure 3: Residues interacting with rosmarinic acid forming Hydrogen bonds (black dash lines) in (a) COVID-19 main protease protein; (b) spike glycoprotein of SARS-CoV-2.

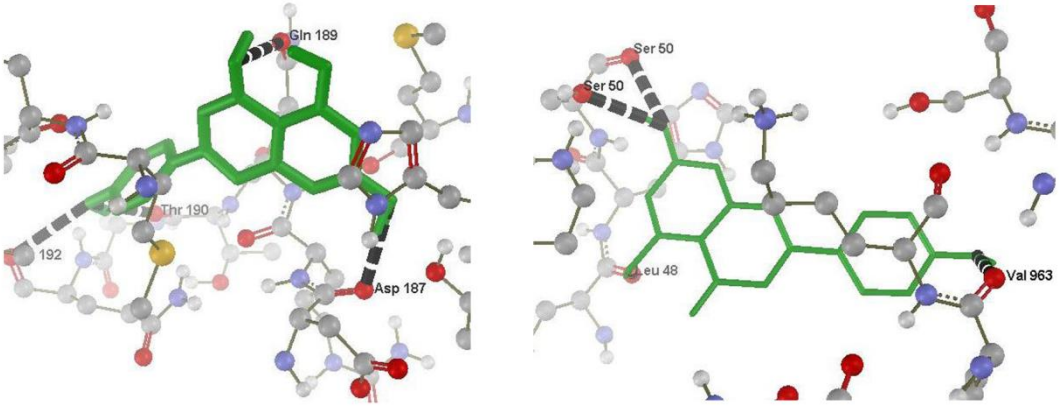

Figure 4: Residues interacting with Apigenine forming Hydrogen bonds (black dash lines) in (a) COVID-19 main protease protein; (b) spike glycoprotein of SARS-CoV-2.

Table 4
ADMET properties of the best results compounds

Ligand	HIA[a] (%)	(Two models were employed for HIA)		PPB[d] (%)	BBB[e] (C.brain/C.blood)	CYP_3A4_ inhibition	CYP_3A4_ Substrate
		CaCo-2[b] (nm/sec)	MDCK[c] (nm/sec)				
*Remdisvir	45.17	1.309	0.049	49.67	0.034	Inhibitor	Substrate
Rosmarinic acid	62.48	20.72	0.202	86.24	0.104	Inhibitor	Non-Substrate
Apigenine	88.12	10.54	44.30	97.25	0.565	Inhibitor	Non-Substrate

[a] HIA stands for Human Intestinal Absorption. [b] CaCo-2 refers to Human colon adenocarcinoma cells. [c] MDCK stands for Madin-Darby canine kidney cells. [d] PPB represents Plasma Protein Binding. [e] BBB stands for Blood Brain Barrier.
*Drug compound.

Oral drug administration necessitates efficient absorption and transport to the bloodstream to achieve therapeutic efficacy. A drug's overall bioavailability depends on factors such as plasma solubility, membrane permeability, protein binding, transport properties and diffusion kinetics. These parameters were calculated using preADMET for the three ligands, including the reference drug, as shown in table 4. The total bioavailability and absorption in urine, bile and feces are determined using the ratio of excretion or cumulative excretion in these fluids, which represents the main obstacle in achieving good bioavailability[38].

This percentage, obtained from preADMET at pH 7.4, revealed that the ligands protocatechuitbdms, oleandrin, epicatechingallate, jervine and piperine are well absorbed compounds, with absorption percentages of >70%.

In assessing the intestinal absorption characteristics of potential drug candidates, various *in vitro* techniques are utilized. Human colon adenocarcinoma (Caco-2) and Madin-Darby canine kidney cells (MDCK) are widely regarded and dependable models for forecasting oral drug absorption. Caco-2 cells, obtained from human colon adenocarcinoma, have numerous pathways for transporting drugs through the intestinal epithelium. Low permeability compounds are those with Pcaco-2 (nm/sec) values less than 4. Caco-2 values between 4 and 70 indicate middle permeability while values greater than 70 indicate highly permeable compounds. The drug compound remdisvir had low permeability in our study, while two ligands had middle permeability in the Caco-2 model. However, rosmarinic acid ligands had low permeability in the MDCK model, as compounds with PMDCK (nm/sec) values less than 25 are low permeable.

The blood brain barrier (BBB), which is primarily made up of tightly bound brain capillaries, astrocytes and other cells, prevents drug-like molecules from entering the brain. The BBB's permeability is an important criterion for CNS activity. BBB values greater than 2.0 indicate high absorption, those between 2.0 and 0.1 percent indicate middle absorption and those less than 0.1 percent indicate low absorption to the CNS[22]. Rosmarinic acid and apigenine ligands had middle absorption.

PPB (Plasma Protein Binding) is a pharmacokinetic criterion that influences the extent of distribution. The drug molecule forms a complex with plasma protein that is pharmacokinetically and pharmacodynamically inert. On the flip side, minimal PPB binding results in a low volume of

distribution and rapid excretion, which hinders the therapeutic effect. Chemicals that have PPB values exceeding 90%, demonstrate strong binding whereas those with PPB values below 90%, exhibit weak binding[19]. Ligand apigenine has shown more than 90% PPB binding which infers them as strongly bound compounds to the plasma. CYP 3A4 plays a major role in drug metabolism[13]. Ligand rosmarinic acid and apigenine have shown inhibitor of CYP 3A4.

Conclusion

This *in silico* investigation revealed that Ocimum aroma compounds are potent inhibitors of Spike Glycoprotein and Protease 3CLpro. Rosmarinic acid and apigenine, as well as the reference medication remdesivir, demonstrated good docking scores with both targets. Their inhibitory potential was also suggested by the H-Bond interaction profile. Various pharmacokinetic parameters such as oral absorption, plasma protein binding, potential metabolic pathways by different CYP enzymes and potential CYP inhibition were evaluated, indicating that the two compounds are pharmacologically active.

As a result, rosmarinic acid and apigenine have a strong potential for use in SARS-CoV-2 treatment. It might be inferred that verification through *in vitro* and *in vivo* studies is required, which could support our investigations.

References

1. Astani A., Reichling J. and Schnitzler P., Comparative study on the antiviral activity of selected monoterpenes derived from essential oils, *Phytotherapy Research*, **24(5)**, 673-679 **(2010)**

2. Behbahani M., Mohabatkar H. and Soltani M., Anti-HIV-1 activities of aerial parts of Ocimum basilicum and its parasite Cuscuta campestris, *Journal of Antivirals & Antiretrovirals*, **5(3)**, 57-61 **(2013)**

3. Belouzard S., Millet J.K., Licitra B.N. and Whittaker G.R., Mechanisms of coronavirus cell entry mediated by the viral spike protein, *Viruses*, **4(6)**, 1011-33 **(2012)**

4. Benencia F. and Courréges M.C., *In vitro* and *in vivo* activity of eugenol on human herpes virus, *Phytotherapy Research*, **14(7)**, 495-500 **(2000)**

5. Caamal-Herrera I.O., Muñoz-Rodríguez D., Madera-Santana T. and Azamar-Barrios J.A., Identification of volatile compounds in essential oil and extracts of Ocimum micranthum Willd. leaves using GC/MS, *International Journal of Applied Research in Natural Products*, **9(1)**, 31-40 **(2008)**

6. Chiang L.C., Ng L.T., Cheng P.W., Chiang W. and Lin C.C., Antiviral activities of extracts and selected pure constituents of Ocimum basilicum, *Clinical and Experimental Pharmacology and Physiology*, **32(10)**, 811-816 **(2005)**

7. Chung Y.C., Hsieh F.C., Lin Y.J., Wu T.Y., Lin C.W., Lin C.T., Tang N.Y. and Jinn T.R., Magnesium lithospermate B and rosmarinic acid, two compounds present in Salvia miltiorrhiza have potent antiviral activity against enterovirus infections, *European Journal of Pharmacology*, **755**, 127-133 **(2015)**

8. Gehlhaar D.K., Bouzida D. and Rejto P.A., Proceedings of the Seventh International Conference on Evolutionary Programming **(1998)**

9. Hilgenfeld R., From SARS to MERS: crystallographic studies on coronaviral proteases enable antiviral drug design, *The FEBS Journal*, **281(18)**, 4085-96 **(2014)**

10. Ikeda K., Tsujimoto K., Uozaki T., Nishide M., Suzuki Y., Koyama A.H. and Yamasaki H., Inhibition of multiplication of herpes simplex virus by caffeic acid, *International Journal of Molecular Medicine*, **28(4)**, 595-598 **(2011)**

11. Irvine J.D., Takahashi L., Lockhart K., Cheong J., Tolan J.W., Selick H.E. and Grove J.R., MDCK (Madin–Darby canine kidney) cells: A tool for membrane permeability screening, *Journal of Pharmaceutical Science*, **88(1)**, 28-33 **(1999)**

12. Jeffrey G.A., An introduction to hydrogen bonding, Oxford University Press, USA **(1992)**

13. Kacevska M., Robertson G.R., Clarke S.J. and Liddle C., Inflammation and CYP3A4-mediated drug metabolism in advanced cancer: impact and implications for chemotherapeutic drug dosing, *Expert Opinion on Drug Metabolism & Toxicology*, **4(2)**, 137-149 **(2008)**

14. Kolita B., Borah D., Hazarika P., Phukan E. and Borah R., Plant-derived Antiviral Compounds as Potential COVID-19 Drug Candidates: In-silico Investigation in Search of SARS-CoV-2 Inhibitors, *Trends in Sciences*, **20(9)**, 5529 **(2023)**

15. Kolita B., Bora A.J. and Hazarika P., A Search of COVID-19 main Protease Inhibitor from Plant Derived Alkaloids using Chloroquine and Hydroxychloroquine as Reference: An *In-silico* Approach, *International Journal of Scientific Research in Biological Science*, **7(2)**, 51-61 **(2020)**

16. Kolita B., Das A.K., Borah D., Hazarika P. and Phukan E., Study of anticancer properties of tea (Camellia sinensis) against lung and breast cancer: an *in-silico* approach of drug design, *International Journal of Biology, Pharmacy and Allied Sciences*, **12(3)**, 1257-1273 **(2023)**

17. Kolita B., Gogoi D., Dutta P.P., Bordoloi M. and Bezbaruah R.L., Arabinosyl transferase inhibitor design against Mycobacterium tuberculosis using ligand based drug design approach, *Bangladesh Journal of Pharmacology*, **9(2)**, 225-229 **(2014)**

18. Kubiça T.F., Alves S.H., Weiblen R. and Lovato T.L., *In vitro* inhibition of the bovine viral diarrhoea virus by the essential oil of Ocimum basilicum (basil) and monoterpenes, *Brazilian Journal of Microbiology*, **45(1)**, 209-214 **(2014)**

19. Lipinski C.A., Lombardo F., Dominy B.W. and Feeney P.J., Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings, *Advanced Drug Delivery Review*, **1(46)**, 3-26 **(1997)**

20. Liu X., Zhang B., Jin Z., Yang H. and Rao Z., The crystal structure of COVID-19 main protease in complex with an inhibitor N3, Protein Data Bank, 6LU7 **(2020)**

21. Lotfi H., Mazar M.G., Ei N.M.H., Fahim M. and Yazdi N.S., Vaccination is the most effective and best way to avoid the disease of COVID-19, *Immunity Inflammation Disease*, **11(18)**, e946 **(2023)**

22. Ma X.L., Chen C. and Yang J., Predictive model of blood-brain barrier penetration of organic compounds, *Acta Pharmacologia Sinica*, **26(4)**, 500-512 **(2005)**

23. Mohamed S., Saini M., Sharma B., Gupta L.K. and Gupta P.K., Ocimum tenuiflorum possesses antiviral activity against bovine herpes virus-1, *Indian Journal of Virology*, **17(28)**, 28-34 **(2006)**

24. Mukhtar M., Arshad M., Ahmad M., Pomerantz R.J., Wigdahl B. and Parveen Z., Antiviral potentials of medicinal plants, *Virus Research*, **131(2)**, 111-120 **(2008)**

25. Nagai A., Lígia M.L. and Déborah Y.A.C., Influence of viral infection on essential oil composition of Ocimum basilicum (Lamiaceae), *Natural Product Communication*, **6(8)**, 1189-1192 **(2011)**

26. Orhan I.E., Özçelik B., Kartal M. and Kan Y., Antimicrobial and antiviral effects of essential oils from selected umbelliferae and labiatae plants and individual essential oil components, *Turkish Journal of Biology*, **36(3)**, 239-246 **(2012)**

27. Pilau M.R., Alves S.H., Weiblen R., Arenhart S., Cueto A. and Lovato L.T., Antiviral activity of the Lippia graveolens (Mexican oregano) essential oil and its main compound carvacrol against human and animal viruses, *Brazilian Journal of Microbiology*, **42(4)**, 1616-1624 **(2011)**

28. Rajendran H.A.D., Malgija B., Ebenezer N.S., Maheswari U., Victor Roch G., Priyakumari J. and Ignacimuthu S., Homology modeling and molecular docking studies of Purple acid Phosphatase from Setaria italica (Foxtail millet), *International Journal of Scientific Research in Biological Sciences*, **5(4)**, 119-124 **(2018)**

29. Sekar K., Thangaraj S., Saravana S.B., Harisaranraj R. and Suresh K., Phytochemical constituent and antioxidant activity of extract from the leaves of Ocimum basilicum, *Journal of Phytology*, **1(6)**, 408-413 **(2009)**

30. Shargel L. and Yu A.B.C., Applied Biopharmaceutics & Pharmacokinetics, McGraw-Hill, New York **(2005)**

31. Sharma A., Kathuria D., Kolita B., Gohain A., Das A.K., Bhardwaj G. and Simal-Gandara J., Greener approach for the isolation of oleanolic acid from Nepeta leucophylla Benth. its derivatization and their molecular docking as antibacterial and antiviral agents, *Heliyon*, **9(8)**, e18639 **(2023)**

32. Silva M.G.V., Vieira I.G.P., Mendes F.N.P., Albuquerque I.L., Santos R.N. dos, Silva F.O. and Morais S.M., Variation of ursolic acid content in eight Ocimum Species from Northeastern Brazil, *Molecules*, **13(10)**, 2482-2487 **(2008)**

33. Sophie A.A., Aworet-Samseny R.R.R. and Mba C.E.M., Some properties of the medicinal plants essential oils of Gabon, *Phytothérapie*, **13(5)**, 283-287 **(2014)**

34. Thomsen R. and Christensen M.H., MolDock, a new technique for high-accuracy molecular docking, *Journal of Medicinal Chemistry*, **49(11)**, 3315-3321 **(2006)**

35. Wrapp D., Wang N., Corbett K.S., Goldsmith J.A., Hsieh C.L., Abiona O., Graham B.S. and McLellan J.S., Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation, *Science*, **367(6483)**, 1260-1263 **(2020)**

36. Xu X., Chen P., Wang J., Feng J., Zhou H., Li X., Zhong W. and Hao P., Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission, *Science China Life Sciences*, **63(3)**, 457-460 **(2020)**

37. Yamashita S., Furubayashi T., Kataoka M., Sakane T., Sezaki H. and Tokuda H., Optimized conditions for prediction of intestinal drug permeability using Caco-2 cells, *European Journal of Pharmaceutical Sciences*, **10(3)**, 195-204 **(2000)**

38. Yang Z., Wu N., Fu Y., Yang G., Wang W., Zu Y. and Efferth T., Anti-Infectious Bronchitis Virus(IBV) activity of 1,8-cineole: Effect on Nucleocapsid (N) protein, *Journal of Biomolecular Structure and Dynamics*, **28(3)**, 323-330 **(2010)**

39. Zhao Y.H., Le J., Abraham M.H., Hersey A., Eddershaw P.J., Luscombe C.N., Butina D., Beck G., Sherborne B., Cooper I. and Platts J.A., Evaluation of human intestinal absorption data and subsequent derivation of a quantitative structure-activity relationship (QSAR) with the Abraham descriptors, *Journal of Pharmaceutical Science*, **90(6)**, 749-784 **(2001)**.

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