IJPSR (2023), Volume 14, Issue 3 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 23 July 2022; received in revised form, 26 August 2022; accepted 09 September 2022; published 01 March 2023

STUDY ON MOLECULAR DOCKING OF 'NUCLEOCAPSID (N) PROTEIN OF SARS-COV-2' AND 'MCF-7'

M. Shree Legha and Amtuz Zehra

P.G. & Research Department of Zoology, Justice Basheer Ahmed Sayeed College for Women, Teynampet, University of Madras, Chennai - 600018, Tamil Nadu, India.

Keywords:

Molecular docking, Binding energy, SARS-CoV-2, Antivirals, MCF-7, Anticancers

Correspondence to Author:
Dr. Amtuz Zehra

Assistant Professor,
P.G. & Research Department of Zoology, Justice Basheer Ahmed Sayeed College for Women, Teynampet, University of Madras, Chennai - 600018, Tamil Nadu, India.

E-mail: zehraamtuz887@gmail.com

ABSTRACT: The process of eliminating viral infection and massive control from spreading furthermore by any variants may lead to a pandemic in the near future. On the other aspect, the impact of eradicating by the initial stage to prevent, treat carcinoma to decline the affected and death rate to maximum amount by Molecular Docking. The quickest and easiest method to search out the potential drugs is by analyzing the ligand-protein interactions compared to the traditional ways. Drugs of antivirals and anti-cancer drugs are given for treating viral infections and cancers. Massive kinds of viruses affect humans with several diseases, from self-curable diseases to acute mortal diseases. In cancer, the diseases are known by the cells within humans; multiplication occurs and forming the tumors of malignant cells with the flexibility to be a pathological process. Herbal medicines are known to play enormous role by giving initial priority. Various plant species are being employed to cure or prevent viral infections and cancers. Molecular docking provides a fast understanding of the ligand's exploration of conformations, poses among drug targets' binding sites, and predicts the binding affinity of protein-ligand. Its main approach is to spot top-ranked conformations on compounds and means of docking to the active site of target of interest. Intake of naturally suggested fruits and vegetables leads to the goal of decreasing the death rate, and the count of females who are liable to breast cancers.

INTRODUCTION: Molecular Docking is an upcoming most beneficial tool for modern drug discovery. Basically, its goal is to predict the unique possible drug candidates for numerous diseases also, it is computationally exhaustive. Its definition is like a bioinformatics approach that involves the predictable stage of the stable complex of a minimum of two or more molecules through their interactions.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(3).1422-34

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.14(3).1422-34

Docking is a computative procedure of discerning a relevant ligand that fits suitably both energetically and geometrically of the proteins' unique binding site. Simple concepts are ligand and protein - how it fits together. In today's world, we are known and read about the pandemic situation only in history. Still, it was shown in the reality of present day-to-day life how powerful it could be in changing everyone's life of the people of the present generation.

The last outbreak of COVID-19 Coronavirus disease occurs in 2019, in China, it was caused by the SARS-CoV-2 virus, which spreads worldwide being the most infectious disease in humans, and deaths were recorded in more than 2.5 million

human deaths worldwide. Recently, there has also been a rapid expansion - of variants of COVID-19. Still, deep research is going on the findings of possible inhibitors and drugs against the virus of SARS-CoV-2. The development of vaccinations has done great remarkable workable in controlling the death rates. However, the presence of viruses and infections in humans and pandemics still exists; as a cure to this, the therapeutic way of treatment is yet to be identified because it is the main fundamental. The general viral mechanism plays an excellent role and may give a hint of a solution against the upcoming pandemics by the newly analyzed intervention [1].

Generally, this SARS-CoV-2 virus has nucleotides of 30,000 where these are encoded with a total of 29 proteins. Out of 29, the most important 5 Proteins (RNA-dependent RNA polymerase, 3C-Like protease, Nucleocapsid, Spike and Papain-Like protease) play a crucial role in their own individual ways in the process of replication of the virus. In this study, we will deal with the protein one among the five listed above, which has the Targeted Protein, the Nucleocapsid (N) protein of SARS- CoV-2. Where this is an RNA-binding protein for the purpose of viral RNA transcription and replication.

During the research, it was found that Nucleocapsid (N) protein - its tail movement made it easier to access the binding site and its phosphate group - binding site - has residues of the large side chain of the virus SARS-CoV-2 compared to the other proteins. Recent studies suggest that antiviral drugs be developed on the potential - therapeutic effect - targeting Nucleocapsid (N) protein is much more effective in SARS-CoV-2. In general, inhibition of SARS-CoV-2 is highly important for blockage of viral replication. Here we will be using the molecular docking approach to identify all possible inhibitors of the targeted protein of SARS-CoV-2 [2, 3]. Breast cancer is considered one of the most common cancers, with a severe death rate worldwide. As per WHO, it was calculable that by the tip of 2020, quite seven [8]. million ladies were diagnosed with carcinoma worldwide. Of these, close to 685,000 deaths were recorded around the world. Of these, close to 521,000 died and in Europe, throughout a similar year, quite 464,000 new cases were diagnosed and close to 131,000 ladies died. In 2014, within the UK, there have been close to fifty-five, 200 new cases of carcinoma (390 men and concerning fifty-four, 800 women), of that, close to one hundred fifty were diagnosed daily in day-after-day life with close to eleven, 400 deaths thanks to this sort of cancer. It's thought-about that one in 9 ladies is going to be diagnosed with carcinoma throughout their life. In 2014, in European countries, nearly twenty-seven 200 folks died of cancer, with 1,791 victims being ladies with carcinoma. Also, close to six 088 new cases of carcinoma were diagnosed in ladies.

There are unit many factors that may be related to carcinoma, like gender, dangerous intake habits and several lifestyles, case history, alcohol or tobacco consumption, lack of breastfeeding, internal secretion treatments, overweight and fleshiness, among others being diagnosed, several patients with carcinoma attempt to modification their intake habits and their several lifestyles [4]. Here the target macromolecule is MCF-7 (Michigan Cancer Foundation-7). It's a normally used carcinoma cell line that multiple teams have propagated for several years.

It proves to be an acceptable model cell line for carcinoma investigations worldwide and those relating to antitumour medicine. It was established in 1973 by Dr. Soule and colleagues at the Michigan Cancer Foundation; wherever their name derives, MCF-7 cells were isolated from the serous membrane effusion of a 69-year-old lady with pathological process unwellness. With time, MCF-7 has created a lot of knowledge of sensible information for patient care than the other carcinoma cell line. It's ER-positive and Lipo-Lutin receptor (PR)-positive and belongs to the Luminal, commonly thought about to own low pathological process potential. The human breast MCF-7 line, though usually treated as one entity, contains an oversized variety of individual phenotypes, most of that represents solely tiny proportions of the entire population. These phenotypes disagree in organic phenomenon profile, receptor expression, and signalling pathway. Despite variations in individual phenotypes' proliferation rate, a balance of multiple phenotypes is somehow maintained throughout the progressive culturing of the road, maybe by some signalling cooperation. The tiny sub-lines within the parental line are often distended beneath

acceptable selective conditions. The continuance of the vitro choice method (6 months or more) is according to the long amount of your time that happens clinically within the development of resistance to anti-estrogen medical care or aromatase inhibitors in carcinoma patients. However, a crucial question with relevant medical care is whether or not the rising sub-lines specific altered receptors and associated signalling pathways [5, 6, 7, 8].

The well-suited Fruits and Vegetables that contain both the antiviral and antitumour properties in each one of the individual fruits & vegetables naturally itself conjointly within the gift state of affairs; these area units recorded as extremely potential sources, the subsequent are: Cranberry (*Vaccinium macrocarpon*), Red Raspberry (*Rubus idaeus*), Black Raspberry (*Rubus occidentalis*), Parsley (*Petroselinum crispum*), Broccoli (*Brassica oleracea var. italica*). In this research, we will be studying the five antivirals' five models against the targeted protein nucleocapsid (N) of SARS-CoV-2 and the anticancers against the targeted protein MCF-7 cell line via software like autodock, swissdock of molecular docking.

MATERIALS AND METHODS: Here, it works on the concept of *in-silico* experiments, which is the use of software for the process of molecular docking, knowing about an interaction between the ligand molecules and the active site of the target protein molecules. The list of required software is as follows:

UCSF Chimera: It is a visualization software tool for any complexes and molecules. Also, the result analysis is done. Multiscale extension will helps in the analysis of macromolecules assemblies - viral coat. Collaborator extension will enable users to share Chimera Analysis details from different sites [9].

Openbabel: This software's purpose is the interconversion of various molecular structures, accepting the types of 110 file format options. It provides like conversion of 2D or 3D structures, searching the conformer, *etc.*, [10].

SwissDock: This is a web-server-based tool that users are free to use worldwide; it does automatic calculations part that is required for the molecular docking process just by providing the parameters and the input methods like uploading files or using code, URL, sequence, name of receptor the target protein and the ligand molecules [11].

AutoDock (with MGL Tools): This software predicts and analyses the Protein-Ligand interactions based on the parameters of the binding score [12]. It follows the technique of an automated docking system, where it generates pre-computed maps having unique criteria leading to a rapid molecular docking process. Also, this type of virtual docking is used in the screening of molecules for the discovery of drugs [13].

Preparation of Protein File:

Protein Data Bank (PDB): It carries all the information on the proteins (macromolecules), especially the 3D structures, shapes, assemblies of complexes, *etc*.; it builds the data by exploring and adding resources and tools for the purpose of education and research works. Using the Protein Data Bank (PDB) download the 3D structure of the targeted Protein molecules in the PDB format file of the following are:

- Crystal Structure of SARS-CoV-2 Nucleocapsid Protein N - Terminal RNA Binding Domain" by searching with the PDB ID: 6M3M.
- Structure of Human MTHFS with 10 - Formyltetrahydrofolate" by searching with the PDB ID: 3HY3.

Water molecules and the ligands that are attached to the protein molecule were removed using dock prep in the chimera software, and the protein molecule was saved in the pdb format file. The polar hydrogen atoms were added to the protein molecule using the autodock software with the help of autodock tools. Subsequently, the files were saved in the pdbqt format.

Preparation of Ligand File:

PubChem: It is an open user-access chemistry database, it is widely used for small molecules like ligands. also it has certain - specific larger molecules and chemically - modified molecules too, it also deals with information like 2D,3D structures, patents, properties, data, *etc*. Using the

PubChem downloaded the 3D structures in the SDF format file of the following ligand molecules:

- Myricetin (C15H10O8) - PubChem CID: 5281672.
- Quercetin (C15H10O7) - PubChem CID: 5280343.
- Ellagic acid (C14H6O8) - PubChem CID: 5281855.
- Apigenin (C15H10O5) - PubChem CID: 5280443.
- Sulforaphane (C6H11NOS2) - PubChem CID: 5350.

The downloaded files were converted to mol2 file format using the chimera software. Then these ligand files were prepared using autodock tools in the autodock software and finally saved in the pdbqt file format for docking analysis.

Preparation of Grid Box - Map File: The amino acids' location as active sites in the receptor region in that the ligand was docked and was determined using autodock tools. For this reason, a three-dimensional map of the grid box was made in the protein molecule region. The determination of this map was based on the type of docking used. A three-dimensional map was made as wide as the size of the active site of the protein molecule covers itself so that the ligand was likely to be docked to all parts of the protein molecule.

SwissDock Docking: In the Swissdock web portal, upload the prepared protein and ligand file with an e-mail address. Once the docking is completed, it will be notified in the e-mail id, denotes the successful completion and redirecting to the web page where docking is done for the complex with a Swissdock-ID. On that page, analyses are done where it will be provided with all the information regarding the docked complex with the structure, and the best-fitted complex will be mentioned at first. Also, it can be viewed in the Chimera software, where the option is provided below on the same web page.

AutoDock Docking: The protein and ligand files are prepared for docking with the Genetic Algorithm's parameters and with the Lamarckian GA's output model (4.2). Then this docking is carried out on Command Prompt to obtain the final docking results made to run the 'autogrid4.exe' and 'autodock4.exe', which generates the various maps, converting the 'gpf file to glg file' and the 'dpf file to dlg file' format respectively. It is a common and important step irrespective of different types of protein.

Analysis: Molecular docking analyses were performed by using the autodock software in ten independent runs for each ligand molecule. The results of the docking calculation were shown in the output in notepad format. The docking results will show the compound with the lowest binding energy when it binds to the target protein to obtain the docking compound's RMSD (root-mean-square distance) value. The ligand molecule's docking conformation was determined by selecting the pose with the highest affinity (most negative Gibbs' free energy of binding).

Visualization: The protein-ligand complexes were visualized using the autodock software that visualizes the docked molecules in charge format. But the main visualization is done using the chimera software, where the polar and hydrophobic interactions between ligand and target protein were characterized, and 2D and 3D illustrations of such interactions were generated.

RESULTS AND DISCUSSION: The ligand compounds which work as both antiviral and anticancer properties exhibit the compounds like Myricetin (3, 5, 7 – Trihydroxy – 2 - (3, 4, 5-trihydroxyphenyl)-4H-1-benzopyran-4-one) is a member of the flavonoid class of polyphenolic compounds, with antioxidant properties that have found in a rich source in an amount of Cranberry fruit. Quercetin (2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one). It is one of the most abundant flavonoids group of polyphenols found in edible vegetables, fruit and wine, which is rich in Red Raspberry fruit. Ellagic acid (2, 3, 7, 8-tetrahydroxy-chromeno [5,4,3-cde] chromene-5,10-dione) is a polyphenol found in several fruits is high in the amount of Black Raspberry fruit. Apigenin (4′, 5, 7,-trihydroxyflavone) is a flavonoid belonging to the flavone structural class found in high amounts in Parsley which is used in vegetables. Sulforaphane is an isothiocyanate

having a 4-(methylsulfinyl) butyl group attached to the nitrogen. It is obtained from cruciferous vegetables and is highly found in Broccoli. The final results of the molecular docking complex (protein-ligand) that was carried on the Swissdock and Autodock are:

In Swissdock:

Protein Molecule: Nucleocapsid (N) Protein of Sars-Cov-2:

FIG. 1: MYRICETIN AND PROTEIN DOCKED COMPLEX

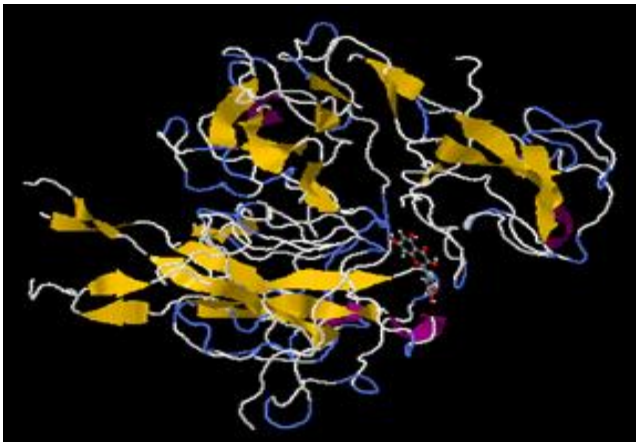

FIG. 2: QUERCETIN AND PROTEIN DOCKED COMPLEX

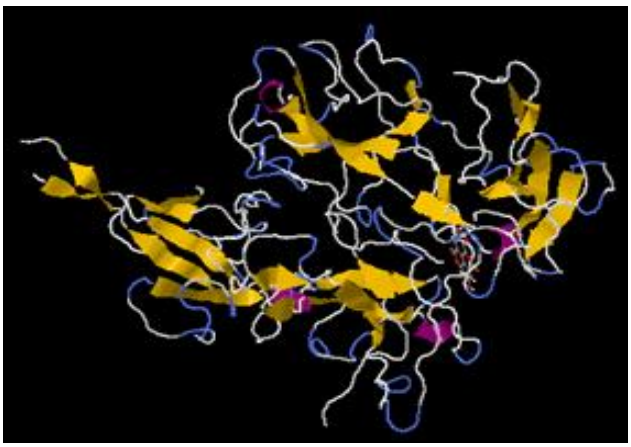

FIG. 3: ELLAGIC ACID AND PROTEIN DOCKED COMPLEX

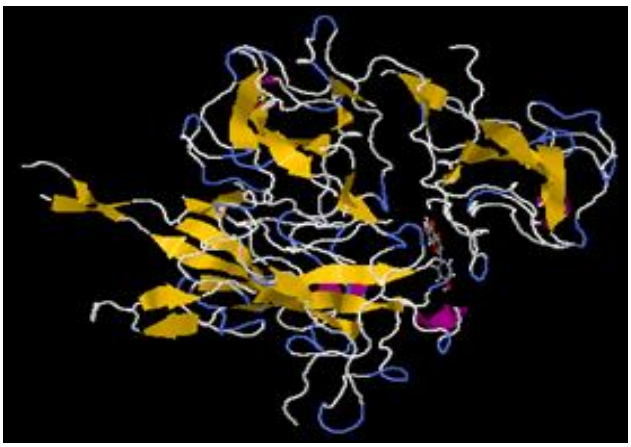

FIG. 4: APIGENIN AND PROTEIN DOCKED COMPLEX

FIG. 5: SULFORAPHANE AND PROTEIN DOCKED COMPLEX

TABLE 1: SWISSDOCK RESULT - VIRAL PROTEIN

S. no.	Target - Protein Molecule	Ligand Molecules	Estimated ΔG (Kcal/Mol)
1.	Crystal Structure Of SARS-CoV-2	Myricetin	-8.15
2.	Nucleocapsid Protein N - Terminal RNA	Quercetin	-7.30
3.	Binding Domain	Ellagic acid	-8.41
4.		Apigenin	-7.36
5.		Sulforaphane	-7.06

Protein Molecule: MCF – 7:

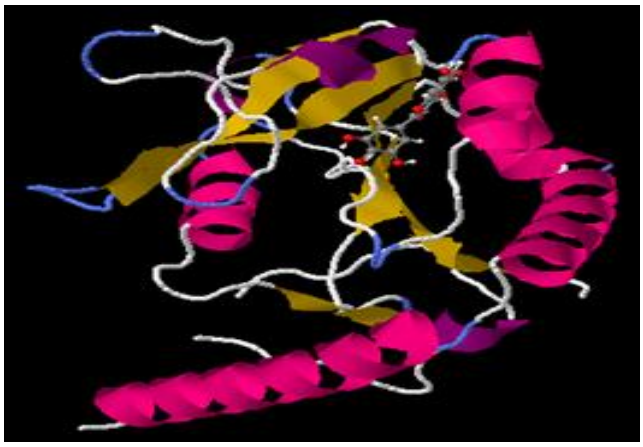

FIG. 6: MYRICETIN AND PROTEIN DOCKED COMPLEX

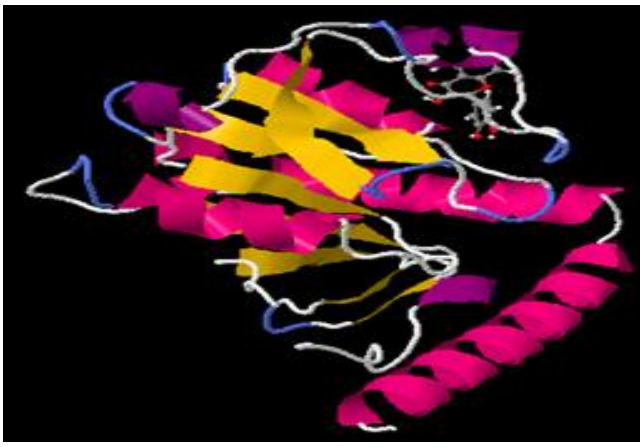

FIG. 7: QUERCETIN AND PROTEIN DOCKED COMPLEX

FIG. 8: ELLAGIC ACID AND PROTEIN DOCKED COMPLEX

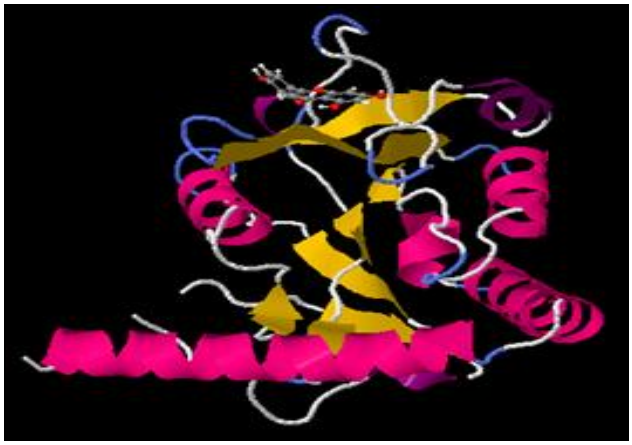

FIG. 9: APIGENIN AND PROTEIN DOCKED COMPLEX

FIG. 10: SULFORAPHANE AND PROTEIN DOCKED COMPLEX

TABLE 2: SWISSDOCK RESULT - CANCER PROTEIN

S. no.	Target - Protein Molecule	Ligand Molecules	Estimated ΔG (Kcal/Mol)
1.	Structure Of Human MTHFS With 10 - Formyltetrahydrofolate	Myricetin	-7.64
2.		Quercetin	-7.65
3.		Ellagic acid	-7.34
4.		Apigenin	-7.13
5.		Sulforaphane	-7.73

In Autodock:

Protein Molecule: Nucleocapsid (N) Protein of Sars-Cov-2:

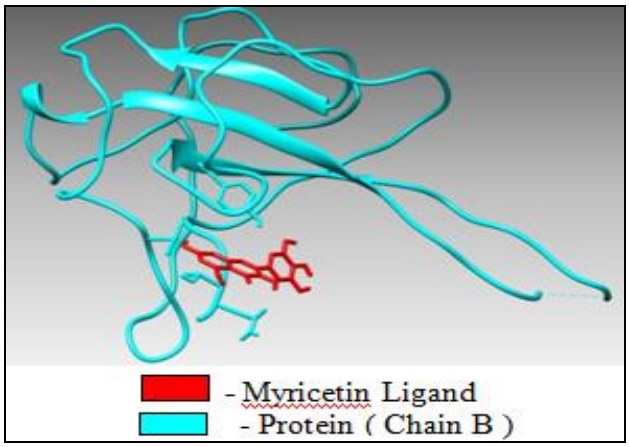

FIG. 11: MYRICETIN AND PROTEIN DOCKED COMPLEX

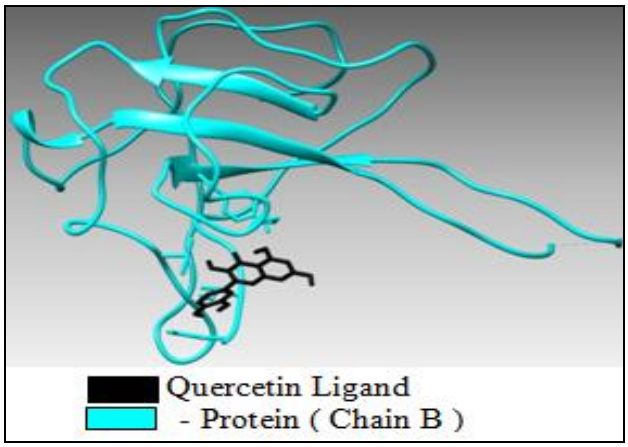

FIG. 12: QUERCETIN AND PROTEIN DOCKED COMPLEX

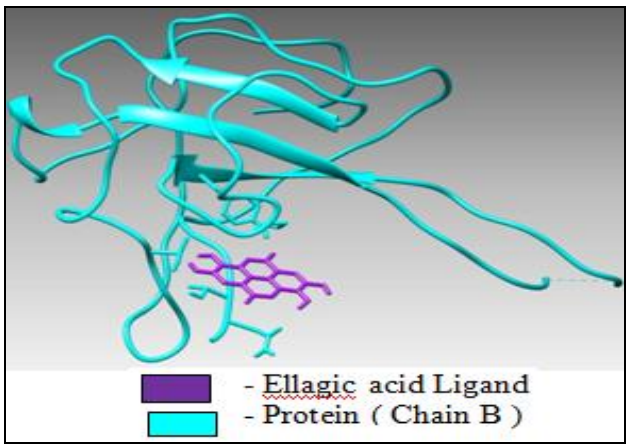

FIG. 13: ELLAGIC ACID AND PROTEIN DOCKED COMPLEX

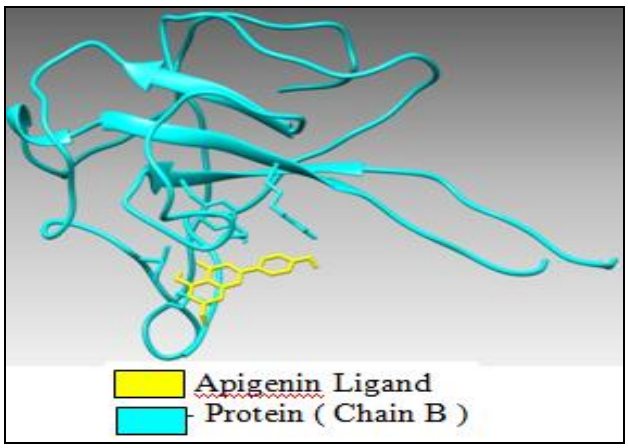

FIG. 14: APIGENIN AND PROTEIN DOCKED COMPLEX

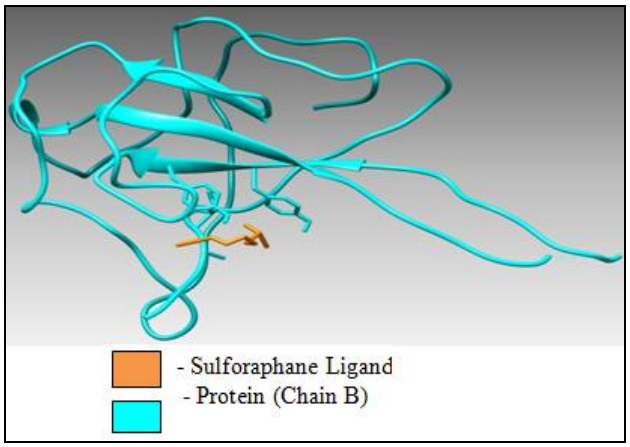

FIG. 15: SULFORAPHANE AND PROTEIN DOCKED COMPLEX

TABLE 3: AUTODOCK RESULT - VIRAL PROTEIN

S. no.	Target - Protein Molecule	Ligand Molecules	Binding Energy - (Kcal/Mol)	No. of Hydrogen Bonds - Formed	No. of Residues Involved	Name of The Residues With Their Positions
1.	Crystal Structure of SARS-CoV-2 Nucleocapsid Protein N - Terminal RNA Binding Domain	Myricetin	-3.68	4	4	Threonine [THR]→50 & UNK→1 (H5, H6, H7).
2.		Quercetin	-3.97	1	1	Tyrosine [TYR]→112
3.		Ellagic acid	-4.84	3	3	Tyrosine [TYR]→112 & UNK→1 (H3, H5).
4.		Apigenin	-4.76	1	1	UNK→1 (H9).
5.		Sulforaphane	-3.53	2	2	Serine [SER]→52 & Tyrosine [TYR]→112

Protein Molecule: MCF – 7:

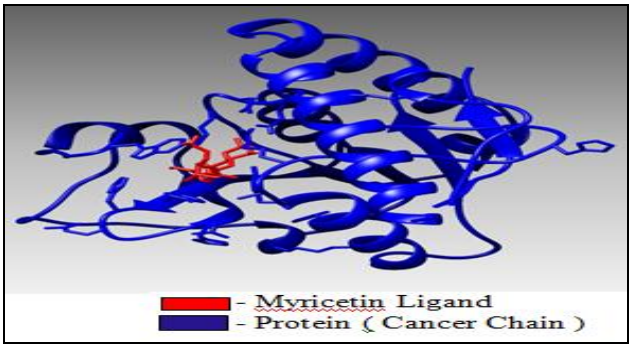

FIG. 16: MYRICETIN AND PROTEIN DOCKED COMPLEX

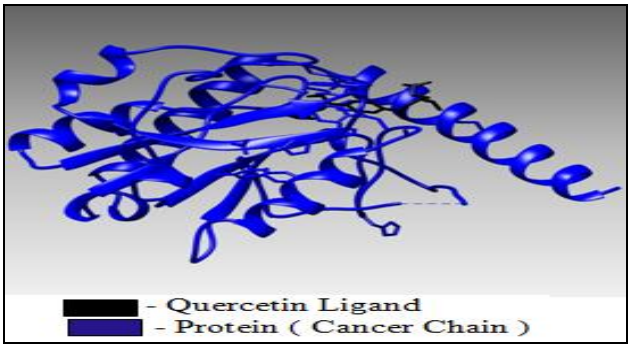

FIG. 17: QUERCETIN AND PROTEIN DOCKED COMPLEX

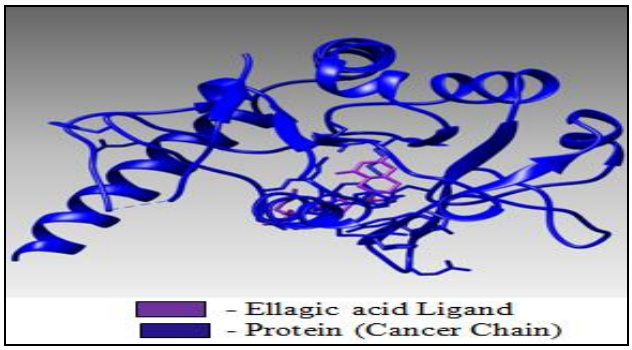

FIG. 18: ELLAGIC ACID AND PROTEIN DOCKED COMPLEX

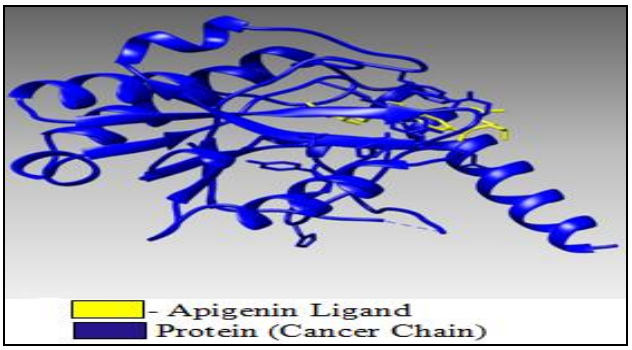

FIG. 19: APIGENIN AND PROTEIN DOCKED COMPLEX

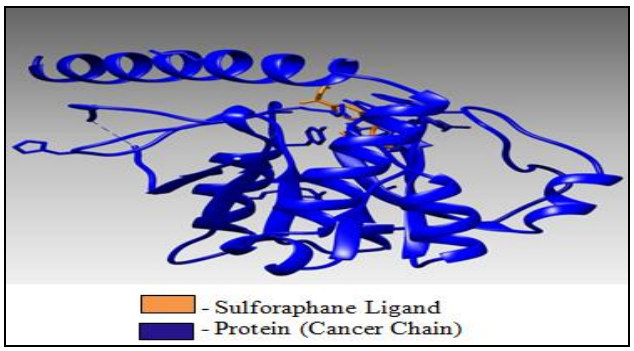

FIG. 20: SULFORAPHANE AND PROTEIN DOCKED COMPLEX

TABLE 4: AUTODOCK RESULT - CANCER PROTEIN

S. no.	Target - protein molecule	Ligand molecules	Binding energy - (kcal/mol)	No. of hydrogen bonds - formed	No. of residues involved	Name of the residues with their positions
1.	Structure Of Human MTHFS With 10 - Formyltetrah -ydrofolate	Myricetin	-4.63	3	3	Arginine [ARG]→14; Glycine [GLY]→147 & UNK→1 (H10).
2.		Quercetin	-4.85	3	3	Glycine [GLY]→147 & UNK→1 (H9, H10).
3.		Ellagic acid	-4.45	1	1	Arginine [ARG]→14.
4.		Apigenin	-4.66	3	3	Glycine [GLY]→147 & UNK→1 (H9,H10).
5.		Sulforaphane	-5.45	4	4	Arginine [ARG]→14 &Glycine[GLY]→147,149,151.

The Binding Site of RNA on the Nucleocapsid (N) protein of SARS-CoV-2 and the Human MTHFS of MCF-7 is taken to be the active site region. The docking is done with the most stable conformation with the least binding energy of the ligand molecules selected that can bind with the protein. This site is considered a therapeutic way and has a high significance. Therefore it is always given the first priority and the second priority goes to the stability of the complex.

Coronavirus: In that case, the most stable complex at the RNA binding site found in the Swissdock portal, Ellagic acid being the highest one, and the second falls on the Myricetin then the Apigenin and being Quercetin is fourth and the least hierarchical order falls for the Sulforaphane. Similarly, in the Autodock, the results are the highest for the Ellagic acid, the second falls on the Apigenin, then for the Quercetin, and Myricetin is fourth and the least hierarchy order falls for the Sulforaphane. Here overall, it can be observed that both in Swissdock and Autodock, Ellagic acid got the highest record and the least for Sulforaphane. Therefore in this study, the most stable complex at the RNA binding site, the well-fitted ligand complex, and the best antiviral compound among the above-mentioned ligands for the SARS-CoV-2 is the Ellagic Acid. Ellagic acid is effective in the treatment of COVID-19 against SARS-CoV-2. This agent has antiviral effects. Its effectiveness on respiratory disease A(H3N2), of three rhinoviruses, HRV-2, HRV-3, and HRV-4, ebola, HIV-1, HSV-1, and noroviruses has been shown. It's antioxidant, medicament, and anti-allergic effects. Curiously this phenol features a synergistic result with anti-malarial medicine. An anti-malarials area unit is currently considered within the treatment protocol for COVID-19.

Ellagic acid features a protecting role in treating respiratory organ harm by modulating inhibitor activities, programmed cell death induction, and inhibiting inflammatory mediators. In a very study on mice with acute respiratory organ injuries, ellagic acid showed medicament effects by decreasing anti-inflammatory drug. Ellagic acid has small tube-shaped structure permeableness alterations and also the white corpuscle enlisting in the bronchoalveolar fluid. It reduced IL-6 and enlarged IL-10 within the bronchoalveolar fluid. As a result, ellagic acid is a unique and safe adjuvant drug for SARS-CoV-2 COVID-19 [14]. Myricetin - the binding created of myricetin with SARS-CoV-2 was known to exploit the molecular docking technique. Within the binding pocket of SARS-CoV-2, the chromone ring of Myricetin interacts with His41 through π-π stacking, and also the 3'-, 4'- and 7-hydroxyl of Myricetin act with Phe140,

Glu166, and Asp187 through element bonds. Considerably, our results showed that Myricetin contains a potent result on bleomycin-induced pneumonic inflammation by inhibiting the infiltration of inflammatory cells and also the secretion of inflammatory cytokines IL-6, IL-1α, TNF-α, and IFN-γ. Overall, Myricetin is also a possible drug for anti-virus and symptomatic treatment of COVID-19. Apigenin with chemicals created from plants have inhibitor, anticancer, medicament, and anti-hyperglycemic activities and was used as compound in drug discovery. Recent studies have conjointly shown the antiviral effectiveness of apigenin against many viruses. Additionally, it had been evidenced and represented that apigenin has antiviral effects against the SARS-CoV-2 coronavirus. The pharmacological medicine and toxicity properties of the ligand compound apigenin analogs with the simplest binding energies were evaluated as potential drug candidates.

Quercetin - the severe acute metabolic process syndrome coronavirus a pair of (SARS-CoV-2) is the reason behind the continuing world pandemic called COVID-19 supported the potential antiviral role of quercetin. On its represented anti-blood natural action, medicament, and inhibitor properties, tend to expect that subjects with gentle COVID-19 treated with Quercetin Phytosome (QP), a unique bioavailable style of quercetin, could have a shorter time to virus clearance, milder symptomatology, and better possibilities of a benign earlier resolution of the diseases. Conjointly statistically shortens the temporal arrangement of the molecular take a look at conversion from positive to negative, reducing at the constant time symptoms severity and negative predictors of COVID-19 [15].

Sulforaphane was a promising candidate to focus on the host cellular response. It is orally bioavailable, commercially available at a low value, and has restricted facet effects. We tend to discover that SFN has twin antiviral and anti-inflammatory properties against coronaviruses. We tend to determine that SFN has potent antiviral activity against multiple strains of SARS-CoV-2, together with Delta and Omicron, with restricted toxicity in cell culture. The similar results discovered between the coronaviruses evaluated recommend that SFN might have broad activity against coronaviruses. This feature will prove priceless as new strains of infective coronaviruses enter the human population [16].

Breast Cancer: In the second case, the most stable complex at MTHFS binding site that found in the Swissdock portal, Sulforaphane being the highest one and the second falls on Quercetin then for the Myricetin and being Ellagic acid is fourth and the least hierarchical order falls for the Apigenin. Similarly, in the Autodock, the results are the highest for the Sulforaphane and the second falls on Quercetin, then for Apigenin and being Myricetin is fourth and the least hierarchy order falls for the Ellagic acid. Here overall, it can be observed that both in Swissdock and Autodock, Sulforaphane got the highest record and the least for the Ellagic acid.

Therefore in this study, the most stable complex at MTHFS binding site, the well-fitted ligand complex, and the best anticancer compound among the above-mentioned ligands for the MCF-7 is Sulforaphane. Sulforaphane is wealthy in Broccoli and is an associated antioxidative and anti-inflammatory compound found in cruciferous vegetables which modulates numerous cellular targets concerned with cancer development. It suppresses MMP-9 expression and invasion in MCF-7 cells *via* inhibition of NF-KB. Also, all of the chemopreventive actions of sulforaphane in breast and prostatic adenocarcinomas are because of the modification of epigenetic mechanisms. Co-treatment of sulforaphane and Withaferin A synergistically induced cell death and reduced cell viability and epigenetic processes in carcinoma cell lines.

It's been shown to induce cell death in carcinoma, prostate cancer, carcinoma, cancer of the liver, and carcinoma in mice. Though the advantages of sulforaphane are tried in cell-based, animal, and a few human trials, recommendations are few. Hence, Sulforaphane use is proscribed as an associate adjuvant to standard chemotherapy and radiotherapy. It's going to be useful in preventing repeats among head-and-neck cancer survivors. Sulforaphane helps in protecting against chronic exposure to environmental pollutants and carcinogens. Recent studies involving mice, furthermore as humans located some adverse

effects on the utilization of this substance. Sulforaphane is believed to cause autophagy in cancer cells [17]. Quercetin could be a dietary flavonoid that exerts antioxidant, medication, and anti-cancer properties. The anti-proliferative result of quercetin in carcinoma cell lines MCF-7 differed in internal secretion receptors. MCF-7 cells on quercetin treatment showed a lot of apoptotic cells with G1 phase arrest. Additionally, quercetin effectively suppressed the expression of Cyclin D1, p21, Twist, and phospho p38MAPK. The quercetin evoked cell death in MCF-7 cells was confirmed by Transmission Electron Microscopy, wherever the cells showed a lot of range of broken cells with chromatin granule condensation and autophagic in distinction to manage MCF-7 cells that showed a standard design with a structured nucleus, organelle, and microvilli representing a proliferating cell. Thus, quercetin acts as a possible anti-breast cancer agent in sex hormone receptor-positive carcinoma [18].

Myricetin belongs to the polyphenol flavonoid with nutraceutical values that is profusely found because of the main ingredient of assorted foods and beverages. It's been reported that the perform of myricetin is to trigger programmed cell death in many forms of cancers. The current study is meant to analyze the apoptotic effects of myricetin on MCF-7 carcinoma cells and to assess its attainable mechanisms of action. The expression levels of apoptosis-related genes caspase-3, caspase-8, caspase-9 and also the BAX /Bcl-2 quantitative relation additionally because the expression of p53, BRCA1, GADD45 genes were considerably exaggerated following the treatment of MCF-7 carcinoma cells with myricetin. It expeditiously induces programmed cell death in MCF-7 carcinoma cells by evoking each adscititious and intrinsic apoptotic pathway. Myricetin could exert its apoptotic effects on MCF-7 cells [19].

Ellagic acid has a tendency that inhibits the proliferation of MCF-7 carcinoma cells principally mediate by the sensational cell cycle within the G0/G1 section. TGF-β/Smads sign pathway was also found because of ellagic acid's potential molecular mechanism to control cell cycle arrest in vitro. Therefore, the regulation of the TGF-β/Smads pathway in carcinoma cells may be a unique therapeutic approach for the treatment of patients with carcinoma. Additional studies with in vivo models, still as associate degree analysis of extra-human samples square measure still required to verify the molecular mechanisms of ellagic acid in inhibition or hindrance of carcinoma growth. It's gained wide attention for cancer medical aid because of its wide biological activities and totally different molecular targets. It has a low chemical reaction and lipotropic and hydrophobic nature isn't ready to be absorbed in circulation. So, accumulation within the internal organ of animal tissue cells or metabolization to different urolithins ends up in the limitation of direct analysis of ellagic acid effects in clinical records. The results demonstrate ellagic acid modulates the expression of varied genes incorporated within the cancer-related method of caspase-mediated cell death and proliferation, inflammation related-gens and oxidative-related genes.

Moreover, the ellagic acid formulation in carriers composed of lipoid, silica, chitosan, iron- bovine albumen nanoparticles clearly increased the stable unharness and assured delivery with minimum loss. Also, *in-silico* analysis verified that ellagic acid was ready to be placed at a foothold of cocrystal ADP, within the deep cavity of the macromolecule target, and tightly move with binding pocket residues resulting in suppression of substrate availableness of the macromolecule. Apigenin, a dietary flavonoid, has been reportable as an associate degree antitumor drug *in-vivo* and *in-vitro*. Within the present study, we have a tendency to investigate whether or not apigenin is in a position to reverse drug resistance victimization using carcinoma cells (MCF-7). In our experiments, apigenin considerably reduced cell growth and colony formation in MCF-7 cells and parental MCF-7 cells.

This growth inhibition was associated with the buildup of cells within the sub-G0/G1 apoptotic population and a rise in the variety of apoptotic cells. Apigenin reduced the template RNA expression of multidrug resistance one (MDR1) and multidrug resistance-associated proteins (MRPs) in MCF-7 cells [20]. The results showed that eighty μM apigenin may effectively induce caspase-mediated cell death and overrun ROS in MCF-7 cells. Here, atomic force microscopy (AFM) was utilized to notice the shapes and

membrane structures of MCF-7 cells at the cellular or subcellular level. The results showed that the present MCF-7 cells bestowed typical elongated-spindle shapes with extensive pseudopodia, whereas once treated with apigenin the cells shrunken and have become spherical and the pseudopodia diminished. Moreover, the pictures of ultrastructure indicated that the cell wall was composed of nanoparticles of forty-nine nm, however, with the treated concentrations of apigenin increasing, the sizes of membrane particles considerably redoubled to a four-hundred nm measure. These results will improve our understanding of apigenin, which might probably be developed as a brand new agent for the treatment of breast cancers [21]. As an outcome, with the above-used medicinal drug molecules - ligand that can bind to their respective binding site of the proteins, the multiplication of the virus and the cancer cells can be much prevented.

CONCLUSION: The Binding Energy (in kcal/mol) order wise of the ligand molecules that are carried on the molecular docking with the: In Nucleocapsid (N) protein of SARS-CoV-2 that docked on protein-ligand complex in the Swissdock are Sulforaphane (-7.06), Quercetin (-7.30), Apigenin (-7.36), Myricetin (-8.15) and Ellagic acid (-8.41) and that on the Autodock are Sulforaphane (-3.53), Myricetin (-3.68), Quercetin (-3.97), Apigenin (-4.76) and Ellagic acid (-4.84). Similarly, in Human MTHFS of MCF-7 that docked on protein-ligand complex in the Swissdock are Apigenin (-7.13), Ellagic acid (-7.34), Myricetin (-7.64), Quercetin (-7.65) and Sulforaphane (-7.73) and that on the Autodock are Ellagic acid (-4.45), Myricetin (-4.63), Apigenin (4.66), Quercetin (-4.85) and Sulforaphane (-5.45).

Thus, the best-ranking order hierarchy found among the five ligand-docked complex in the SARS-COV-2 records in the Swissdock are Ellagic acid, Myricetin, Apigenin, Quercetin, and followed by Sulforaphane. In the Autodock, records in, Ellagic acid, Apigenin, Quercetin, Myricetin and followed by Sulforaphane. Similarly the best ranking order hierarchy that was found among the five ligand - docked complexes in the MCF-7 that were recorded in the Swissdock are Sulforaphane, Quercetin, Myricetin, Ellagic acid and followed by Apigenin. The Autodock records Sulforaphane, Quercetin, Apigenin, Myricetin and, followed by Ellagic acid. Molecular docking is extremely helpful for investigating, comparing, analyzing and visualizing chemical structures and giving qualitative and quantitative information regarding biological systems. It is accustomed study pure geometric, energy and, therefore the chemical properties *in-silico* that records with efficiency, these days its potential to predict the result of chemical reactions, style reactions, verify the unknown three-dimensional structures of proteins, screen, and style new and effective medicine. All in all, the longer term is bright for molecular docking. New technologies area unit being developed and utilized within the race against drug discovery and deadly diseases. Data processing, machine or deep learning, hyper-computers, and cloud computers area unit simply many of the rising technologies in trendy molecular docking.

This study compares all, and provides the common advantageous effects of both the antiviral against the targeting Nucleocapsid (N) protein of SARS-CoV-2 and the anticancer against the targeting human MTHFS as protein of MCF-7 benefits in three ways:

A. Therapeutic results have a high potential and effective.

B. Increases the development of curable drug molecules against the virus of SARS-CoV-2 and cancer of MCF-7.

C. This docking is one of the initial identification, it gives the important backdrop data for carrying out the further process to treat the diseases and their variants in the upcoming days.

Also, by analyzing these research materials and by utilizing the modern way of molecular docking, this study has concluded that consuming these fruits and vegetables regularly with the required dietary components of nutritional intake naturally imparts us with the sufficient amount of antibiotics in our human body without any artificial forms like vaccines, reduces the risk of getting affected from viral diseases like SARS-COV-2 and cancers like human breast cancer MCF-7. This study also shows that the affected ones can be easily cured, and also the variants of SARS-COV-2 & MCF-7, which can

arise shortly, can also be treated in the upcoming days.

ACKNOWLEDGEMENT: The authors are grateful to the management of J. B. A. S. College For Women, Chennai, for providing facilities to carry out this work.

CONFLICTS OF INTEREST: The authors stated that there are no conflicts of interest relating to the publication of this paper.

REFERENCES:

1. Salzberger B, Buder F, Lampl B, Ehrenstein B, Hitzenbichler F, Holzmann T, Schmidt B and Hanses F: Epidemiology of SARS-CoV-2. Infection 2021; 49(2): 233-239.
2. Brian DA and Baric RS: Coronavirus Genome Structure and Replication. In: Enjuanes, L. (eds) Coronavirus Replication and Reverse Genetics. Current Topics in Microbiology and Immunology. Springer Berlin Heidelberg 2005; 287: 1-30.
3. Kang S, Yang M, Hong Z, Zhang L, Huang Z, Chen X, He S, Zhou Z, Zhou Z, Chen Q, Yan Y, Zhang C, Shan H and Chen S: Crystal Structure of SARS-CoV-2 Nucleocapsid Protein RNA Binding Domain Reveals Potential Unique Drug Targeting Sites. Acta Pharmaceutica Sinica B 2020; 10(7): 1228-1238.
4. Deshpande RR, Tiwari AP, Nyayanit N and Modak M: *In-silico* molecular docking analysis for repurposing therapeutics against multiple proteins from SARS-CoV-2. European Journal of Pharmacology 2020; 886: 173430.
5. Baguley BC and Leung E: Heterogeneity of Phenotype in Breast Cancer Cell Lines. In Gunduz M & Gunduz E (Eds.), Breast Cancer - Carcinogenesis, Cell Growth and Signalling Pathways. Intech Open 2011; 245-256.
6. Shirazi FH, Zarghi A, Kobarfard F, Zendehdel R, Nakhjavani M, Arfaiee S, Zebardast T, Mohebi S, Anjidani N, Ashtarinezhad A and Shoeibi S: Remarks in Successful Cellular Investigations for Fighting Breast Cancer Using Novel Synthetic Compounds. In Gunduz M & Gunduz E (Eds.), Breast Cancer - Focusing Tumor Microenvironment, Stem cells and Metastasis. Intech Open 2011; 85-102.
7. Soule HD, Vazguez J, Long A, Albert S and Brennan M: A human cell line from a pleural effusion derived from a breast carcinoma. JNCI 1973; 51(5): 1409–1416.
8. Sweeney EE, McDaniel RE, Maximov PY, Fan P and Jordan VC: Models and Mechanisms of Acquired Antihormone Resistance in Breast Cancer: Significant Clinical Progress Despite Limitations. Hormone Molecular Biology and Clinical Investigation 2012; 9(2): 143–163.
9. Morris GM, Huey R and Olson AJ: UNIT - Using AutoDock for ligand-receptor docking. Current Protocols in Bioinformatics 2008; 1: 24.
10. Pettersen EF, Goddard TD, Huang CC, Couch GS, Greenblatt DM, Meng EC and Ferrin TE: UCSF Chimera - A visualization system for exploratory research and analysis. Journal of Computational Chemistry 2004; 25(13): 1605-1612.
11. Kitchen DB, Decornez H, Furr JR and Bajorath J: Docking and scoring in virtual screening for drug discovery: Methods and Applications. Nature Reviews Drug Discovery 2004; 3(11): 935-949.
12. O'Boyle NM, Banck M, James CA, Morley C, Vandermeersch T and Hutchison GR: Open Babel: An open chemical toolbox. J of Cheminfo 2011; 3(33): 1-14.
13. Pagadala NS, Syed K and Tuszynski J: Software for Molecular Docking: A Review. Biophysical Reviews 2017; 9(2): 91-102.
14. Namazi M, Saki N and Hadibarhaghtalab M: Ellagic acid as a possible adjuvant treatment for COVID- 19 disease. Authorea 2020.
15. Pierro FD, Iqtadar S, Khan A, Mumtaz SU, Chaudhry MM, Bertuccioli A, Derosa G, Maffioli P, Togni S, Riva A, Allegrini P and Khan S: Potential Clinical Benefits of Quercetin in the Early Stage of COVID-19: Results of a Second, Pilot, Randomized, Controlled and Open-Label Clinical Trial. International Journal of General Medicine 2021; 14: 2807–2816.
16. Ordonez AA, Bullen CK, Villabona-Rueda AF, Thompson EA, Turner ML, Merino VF, Yan Y, Kim J, Davis SL, Komm O, Powell JD, D'Alessio FR, Yolken RH, Jain SK and Brando LJ: Sulforaphane exhibits antiviral activity against pandemic SARS-CoV-2 and seasonal HCoV-OC43 coronaviruses *in-vitro* and in mice. Communications Biology2022; 5: 242.
17. Nandini DB, Rao RS, Deepak BS and Reddy PB: Sulforaphane in Broccoli: The green chemoprevention!! Role in cancer prevention and therapy. Journal of Oral and Maxillofacial Pathology 2020; 24(2): 405.
18. Ranganathan S, Halagowder D and Sivasithambaram ND: Quercetin Suppresses Twist to Induce Apoptosis in MCF-7 Breast Cancer Cells. PLOS ONE 2015; 10(10): e0141370.
19. Sajedi N, Homayoun M, Mohammadi F and Soleimani M: Myricetin Exerts its Apoptotic Effects on MCF-7 Breast Cancer Cells through Evoking the BRCA1-GADD45 pathway. Asian Pacific Journal of Cancer Prevention 2020; 21(12): 3461–3468.
20. Seo HS, Ku JM, Choi HS, Woo JK, Lee BH, Kim DS, Song HJ, Jang BH, Shin YC and Ko SG: Apigenin overcomes drug resistance by blocking the signal transducer and activator of transcription 3 signaling in breast cancer cells. Oncology Reports 2017; 38(2): 715–724.
21. Bai H, Jin H, Yang F, Zhu H and Cai J: Apigenin induced MCF-7 cell apoptosis-associated reactive oxygen species. Scanning 2014; 36(6): 622–631.

How to cite this article:
Legha MS and Zehra A: Study on molecular docking of 'nucleocapsid (N) protein of Sars-Cov-2' and 'MCF-7'. Int J Pharm Sci & Res 2023; 14(3): 1422-34. doi: 10.13040/IJPSR.0975-8232.14(3).1422-34.