Molecular docking analysis on 16 therapeutic ligands of *Ocimum tenuiflorum* L. (Tulasi) and their prospects in drug design for COVID-19

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**ABSTRACT**

The PyRx software and Discovery studio were used in the present molecular docking studies of the 16 ligands of *Ocimum tenuiflorum* L., selected based on their high therapeutic potentials, viz., (E)-6-hydroxy-4,6-dimethylhept-3-en-2-one, Apigenin, Bieugenol, Cirsilineol, Cirsimartinin, β-Caryophyllene epoxide, Dehydrodieugenol B, Eugenol, Fernaldehyde, Isothymoquin, Isothymusin, Linalool, Luteolin, Ocimarin, Rosmarinic acid, and Thymol. Saquinavir was used as a positive control. The binding affinities of the 16 ligands to the main proteases of COVID-19 6LU7 and 6Y2E (critical for viral replication) and their ability to arrest the virus replication were recorded. The binding affinities of the ligands to 6LU7 and 6Y2E ranged from -4.3 and -4.7 kcal/mol (for (E)-6-hydroxy-4,6-dimethylhept-3-en-2-one) to -7.6 (for Rosmarinic acid to both target proteins). While the corresponding values for the control drug Saquinavir were -7.8 and -7.6 respectively. The Rosmarinic acid, in binding with both the proteases (-7.6 and -7.6 kcal/mol) showed six conventional hydrogen bonds, one carbon hydrogen bond (ASP 153 had one conventional hydrogen bond and one carbon hydrogen bond), one Pi-alkyl bond, one Pi-Pi stacked bond, eight van der waals bonds for 6LU7 protease; it formed three conventional hydrogen bonds, two Pi-alkyl bonds, one unfavourable donor – donor bond and 14 van der waals bonds with 6Y2E protease. The control drug – Saquinavir in binding with 6LU7 protease showed 12 van der waals, one alkyl, one Pi-alkyl, one Pi-cation, one Pi-stacked and four conventional hydrogen bonds, which indicates that it has less affinity when compared with Rosmarinic acid. Similarly, the control drug on binding with 6Y2E protease exhibited ten van der waals, four Pi-alkyl, one cation and three hydrogen bonds. The results are in conformity to similar other studies, and herald a promising scope for Rosmarinic acid as lead molecule in the drug discovery for COVID-19.

**KEYWORDS:** COVID-19, Molecular docking, PyRx software, Rosmarinic acid, 6LU7 protease, 6Y2E protease

INTRODUCTION

The COVID-19, an infectious dreadful virus disease, has been pandemic since December 2019, and the unimaginable volume of human casualties witnessed so far has propelled the scientific community to explore the possibilities of developing safe herbal drugs (Chojnacka et al., 2020), either as preventive or curative (Kiran et al., 2020), against the COVID-19 (Sampangi-Ramaiah et al., 2020). The present investigation on 16 therapeutic ligands of *Ocimum tenuiflorum* L., (Vernacular name, “Tulasi” in Tamil) (Singh & Chaudhuri, 2018) the latter being the key ingredient in Kandankathiri Legiyam-a Siddha polyherbal formulation used in respiratory diseases, comprise the binding affinities of them to the two main proteases of COVID-19, viz., 6LU7 (Peele et al., 2020) and 6Y2E, and their ability to arrest the virus replication (Sampangi-Ramaiah et al., 2020). The PyRx software and Discovery studio were used in the study to discover lead molecules for the drug design and explore the possibility of repurposing the popular herbal drug in the treatment of COVID-19 (Trott & Olson, 2010). The COVID-19 proteases, 6LU7 (Sisakht et al., 2021) and 6Y2E, are critical for viral replication and the effective binding of the viral proteases will arrest viral replication and the disease (Sampangi-Ramaiah et al., 2020). Hence, the present investigation was taken up towards achieving this purpose.

Modern medicines of the 21st Century have their origin in traditional herbal medicinal practices. An array of compounds is reported as effective lead molecules in drug design and discovery (Wu et al., 2020). *Ocimum tenuiflorum* L., is documented extensively in Siddha and Ayurveda literature to
cure respiratory diseases (Singh & Chaudhuri, 2018). There are studies on Ocimum tenuiflorum L., to show the presence of several class of phytochemicals (Soni & Sosa, 2013) such as alkaloids, carbohydrates, phenolic compounds, tannins, flavonoids, steroids, and saponins (Siva et al., 2016) such phytochemicals possess antibacterial, antiviral, antifungal, antiprotozoal, antimalarial, anti-helminthic, antidiarrheal, analgesic, antipyretic, anti-inflammatory, antiallergic, antihypertensive activities (Pandey & Sharma, 2010). A total of 41 phytochemicals are reported in Ocimum tenuiflorum L., (Singh & Chaudhuri, 2018) and listed in Table – 1, out of these 41 reported phytochemicals, 23 phytochemicals are available in the PUBCHEM database (Kim et al., 2019) with canonical SMILES (Simplified Molecular Input Line Entry System), so these 23 phytochemicals are initially screened using SWISSADME software (Daina et al., 2017) for their drug-likeness (Bhadran et al., 2021).

MATERIALS AND METHODS

Selection of Ligands using SWISSADME Software

The SWISSADME software reports of 23 phytochemicals were analysed as per Lipinski’s rule of five for druglikeness (Lipinski et al., 2012), of these phytochemicals, Ocimumoside A, Ocimumoside B, Oleanolic acid, Orientin, Stigmasterol, Ursolic acid and Vicenin-2 are the violators of Lipinski’s rule of five for drug design and these molecules were not taken for docking studies.
Whereas, (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one, Apigenin, Bieugenol, Cirsinineol, Cirsimarinin, β-Caryophyllene epoxide, Dehydrodieugenol B, Eugenol, Feruladehyde, Isothymonin, Isothymusin, Linalool, Luteolin, Ocimarin, Rosmarinic acid, and Thymol are non-violaters of Lipinski’s rule of five and hence these 16 molecules (Figure 1) were docked with 6LU7 and 6Y2E main proteases of SARS CoV2 (Figure 2).

**Ligand Preparation**

The input canonical SMILES from PUBCHEM database of these 16 phytochemicals (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one, Apigenin, Bieugenol, Cirsinineol, Cirsimarinin, β-Caryophyllene epoxide, Dehydrodieugenol B, Eugenol, Feruladehyde, Isothymonin, Isothymusin, Linalool, Luteolin, Ocimarin, Rosmarinic acid, and Thymol are utilized to make PDB files through online source https://www.novoprolabs.com/tools/smiles2pdb the output was saved as PDB file for the molecules. The target proteins are 6LU7 and 6Y2E of SARS-CoV-2 (2019) were obtained from https://www.rcsb.org/website in PDB format (Sampangi-Ramaiah et al., 2020).

**PyRx Software and Discovery Studio**

PyRx is software, it is used for molecular docking studies (Dallakyan & Olson, 2015). PyRx docks the compounds available in “Protein Data Base – (PDB)” format online in the data base against potential drug targets (Trott & Olson 2010). It enables pharmacologists to perform simulations for the drug design and discovery process (Raj, 2021). It comprises a docking wizard with easy-to-use user interface which makes it a valuable tool for computer-aided drug design (Chen, 2014). The rational drug design is made possible by this software because of its chemical spreadsheet-like functionality, and powerful visualization engine (Shaker et al., 2020). The software is unique in docking five ligands with the desired target protein (Figure 3). The latter feature of PyRx is explored in the present study (Chaudari et al., 2020). Discovery studio is allied software to PyRx for visualizing the protein database files of ligand and target before and after docking by PyRx (Shaker et al., 2020). It is mandatory that the input files must be in PDB format for both ligand and target protein (Yuliana et al., 2013).

**Preparation of Target Protein and Molecular Docking**

The water molecules and HET atoms of 6LU7 and 6Y2E were eliminated (Figure 2), and the polar hydrogens were added and saved in the system using Discovery studio software. Later, the saved PDB file of the target protein is given as an input file in PyRx software along with the PDB files of the 16 ligands (Figure 1). The files get converted to pdbqt format and then the docking site was confirmed by a grid box with the dimensions (Angstrom) of X: 65.20, Y: 64.98 and Z: 25.00 for 6LU7 protease (Ounthaisong & Tanyuenyongwatana, 2017) and for 6Y2E protease it is X: 51.21, Y:70.17, Z: 25.00 (Herowati & Widodo, 2014) (Figure 3).

The output of the docking score was obtained in CSV format was saved as MS-EXCEL spread sheet for tabulation. The docked
files with RMSD value with zero alone were saved as PDB file and visualized through discovery studio software to comprehend the ligand-protein interactions. It is pertinent to mention here that the RMSD < 2.0 Å provides a good solution, hence docked position with zero was prioritised and saved as PDB file (Figure 3) (Ramírez & Caballero, 2018) for visualization through Biovia discovery studio software. The output of PyRx software results were presented in figures 4-9 and Tables 1-3.

RESULTS AND DISCUSSION

The 16 ligands of Ocimum tenuiflorum L. (Figure 1) chosen based on their drug-likeness as per Lipinski’s rule of five (Lipinski et al., 2012) for drug design and presented in Table 1. The molecular docking studies revealed the values of their binding affinity to 6LU7 and 6Y2E proteases of COVID-19 with a score ranging from -4.3 kcal/mol and -4.7 kcal/mol respectively for (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one of -7.6 kcal/mol for Rosmarinic acid (Table 2 and 3, Figure 1 -9).

The ascending order of binding affinity for the 16 ligands with 6LU7 protease was (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one (C9H16O2) < Linalool (C10H18O) < Thymol (C10H14O) < Ferulaldehyde (C10H10O3) < Eugenol (C10H12O2) < Bieugenol (C20H22O4) < Ocimarin (C12H12O4) < β-Caryophyllene epoxide (C15H24O) < Dehydrodieugenol B

Figure 4: The 2D and 3D Visualization of Docking Analysis of Molecular Interaction of 6LU7 and 6Y2E Protease with (E)-6-hydroxy-4,6-dimethyl-3-heptene-2-one and Apigenin
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(C_{20}H_{22}O_4) < Cirsimaritin (C_{17}H_{14}O_6) < Isothymusin (C_{17}H_{14}O_7) < Apigenin (C_{15}H_{10}O_5) < Cirsilineol (C_{18}H_{16}O_7) < Isothymonin (C_{18}H_{16}O_8) < Luteolin (C_{15}H_{10}O_6) < Rosmarinic acid (C_{18}H_{16}O_8) (Table 1).

The 13 different types of bonding of the 16 ligands with the target protein 6LU7 were recorded. Single C-H bond was evident in the case of Apigenin, Cirsilineol, Cirsimaritin, Dehydroeugenol B, Isothymonin, Isothymusin, Ocimarin and Rosmarinic acid (Table 2). While that of conventional hydrogen bond, Rosmarinic acid displayed six followed by Cirsimaritin with four, cirsilineol with three, and Dehydrodieugenol B, Isothymonin, Isothymusin, and Ocimarin formed two conventional hydrogen bonds each. With regard to the Apigenin it revealed a single conventional hydrogen bond with 6LU7 protease (Table 2). The rest of the ligands did not exhibit such C-H bond and conventional hydrogen bond. It is pertinent to mention here that different types of pi-bonds and van der waals electrostatic attractions are weaker than C-H bond and conventional hydrogen bonds. Thus, it is evident that Rosmarinic acid has a strong binding affinity with 6LU7 than the other 15 ligands (Figure 4-9).

The ascending order of binding affinity of the 16 ligands with 6Y2E protease was (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one (C_{10}H_{16}O_2) < Linalool (C_{10}H_{18}O) < Eugenol (C_{10}H_{12}O_2) < Thymol (C_{10}H_{14}O) < Feraldehyde (C_{10}H_{10}O_2) < Bieugenol (C_{20}H_{22}O_4) < β-Caryophyllene epoxide.

Figure 5: The 2D and 3D Visualization of Docking Analysis of Molecular Interaction of 6LU7 with Bieugenol, Caryophyllene Epoxide, Cirsilineol and 6Y2E Protease with Bieugenol and Caryophyllene Epoxide

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(C_15H_24O) < Dehydrodieugenol B (C_20H_22O_4) < Ocimarin (C_15H_24O) < Isothymusin (C_15H_14O_4) < Cirsimaritin (C_15H_14O_4) < Cirsilineol (C_15H_16O_7) < Isothymonin (C_18H_16O_8) < Apigenin (C_15H_10O_5) < Luteolin (C_15H_10O_6) < Rosmarinic acid (C_18H_16O_8) (Table 1).

The molecular docking results of 16 ligands with 6Y2E protease exhibited that (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one (C_9H_16O_2), Bieugenol, Cirsilineol, Dehydrodieugenol B, Ferulaldehyde and Isothymonin have one C-H bond each. Whereas regarding the formation of conventional hydrogen bonds, Ocimarin has formed four, followed Rosmarinic acid and Ferulaldehyde three each, (E)-6-hydroxy-4,6-dimethyl-3-heptene-2-one (C_9H_16O_2), Eugenol and Luteolin formed two each.

The Apigenin, Bieugenol, Cirsilineol, Dehydrodieugenol B, Isothymonin, Isothymusin, Linalool and Thymol contributed one conventional bond each (Table 3). Although Rosmarinic acid did not formed a C-H bond with 6Y2E protease, but it has three conventional hydrogen bonds, 14 van der Waals electrostatic attractions, two pi-alkyl bonds and one unfavourable donor bond with 6Y2E protease. So, Rosmarinic acid shall be considered as a promising drug candidate to combat SARS CoV2 (Table 3).

The binding affinity of the control drug Saquinavir were -7.8 and -7.6 for 6LU7 and 6Y2E respectively (Table 1). Whereas, that of Rosmarinic acid, in binding with both the proteases the binding affinity were -7.6 and -7.6 kcal/mol. The Rosmarinic acid showed six conventional hydrogen bonds, one carbon hydrogen

Figure 6: The 2D and 3D Visualization of Docking Analysis of Molecular Interaction of 6LU7 with Cirsimaritin, Dehydrodieugenol-B, Eugenol and 6Y2E Protease with Cirsilineol, Cirsimaritin, Dehydrodieugenol-B
Table 1: The 16 ligands of *Ocimum tenuiflorum* and their binding affinity to 6LU7 and 6Y2E proteases of SARS–CoV2

| S.No | Ligand (Molecular formula) | Molecular weight | Binding affinity to 6LU7 (kcal/mol) | Binding affinity to 6Y2E (kcal/mol) |
|------|---------------------------|------------------|-------------------------------------|------------------------------------|
| 1    | (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one | 156.22           | -4.3                                | -4.7                               |
| 2    | Apigenin (C_{15}H_{10}O_{5}) | 270.24           | -6.7                                | -7.4                               |
| 3    | Bieugenol (C_{20}H_{22}O_{4}) | 326.39           | -5.9                                | -5.6                               |
| 4    | Cirsilineol (C_{18}H_{16}O_{7}) | 344.32           | -6.8                                | -6.7                               |
| 5    | Cirsimaritin (C_{17}H_{14}O_{6}) | 314.29           | -6.5                                | -6.6                               |
| 6    | β-Caryophyllene epoxide (C_{15}H_{20}O) | 220.35           | -6                                  | -6                                 |
| 7    | Dehydrodieugenol B (C_{20}H_{23}O_{4}) | 326.39           | -6.1                                | -6.3                               |
| 8    | Eugenol (C_{10}H_{18}O) | 164.20           | -5.5                                | -5                                 |
| 9    | Ferulaldehyde (C_{10}H_{12}O) | 178.18           | -5.4                                | -5.5                               |
| 10   | Isothymonin (C_{15}H_{10}O_{5}) | 360.0            | -6.8                                | -6.7                               |
| 11   | Isothymusin (C_{17}H_{14}O_{7}) | 330.29           | -6.6                                | -6.5                               |
| 12   | Linalool (C_{10}H_{18}O) | 154.25           | -4.5                                | -4.7                               |
| 13   | Luteolin (C_{15}H_{10}O_{5}) | 286.24           | -7.1                                | -7.5                               |
| 14   | Ocimarin (C_{12}H_{12}O_{4}) | 220.22           | -5.9                                | -6.5                               |
| 15   | Rosmarinic acid (C_{18}H_{16}O_{6}) | 360.3           | -7.6                                | -7.6                               |
| 16   | Thymol (C_{10}H_{18}O) | 150.22           | -4.8                                | -5.4                               |
| 17   | Saquinavir (C_{38}H_{50}N_{6}O_{5})* | 670.84         | -7.8                                | -7.6                               |

*Positive Control - Synthetic HIV drug (Megha Hastantram Sampangi-Ramaiah et al., 2020)
Table 2: The 16 ligands of *Ocimum tenuiflorum* and the details of different bonds formed with 6LU7 protease of SARS-CoV2

| S. No | Ligand                          | Van der Waals | C–H | Pi-Alkyl | Pi-Hydrogen | Anion | Pi-Cation | Pi-Sigma | Stacked | T-shaped | Conventional Hydrogen | Unfavourable Acceptor | Unfavourable Donor | Total |
|-------|---------------------------------|---------------|-----|----------|-------------|-------|-----------|----------|---------|----------|------------------------|---------------------|---------------------|-------|
| 1     | (E)-6-Hydroxy-4,6-dimethyl-3-heptene-2-one | 4              | -   | -        | -           | -     | -         | -        | -       | -        | 4                      | -                   | -                   | 8     |
| 2     | Apigenin                        | 7             | -   | 1        | -           | 1     | 1         | 1        | 1       | -        | 4                      | -                   | -                   | 14    |
| 3     | Bieugenol                       | 6             | 2   | 1        | -           | -     | -         | -        | -       | -        | 2                      | -                   | -                   | 11    |
| 4     | Cirsilineol                     | 4             | 1   | 1        | 1           | -     | -         | -        | -       | -        | 3                      | -                   | -                   | 10    |
| 5     | Cirsimaritin                    | 2             | 1   | 1        | 1           | -     | -         | -        | -       | -        | 4                      | -                   | -                   | 9     |
| 6     | β-Caryophyllene epoxide         | 8             | 1   | -        | -           | -     | -         | -        | -       | -        | -                      | -                   | -                   | 9     |
| 7     | Dehydrodieugenol B              | 9             | 1   | 1        | 1           | -     | -         | 2        | -       | 1        | 2                      | -                   | 1                   | 18    |
| 8     | Eugenol                         | 5             | 1   | -        | -           | -     | -         | -        | -       | -        | 2                      | -                   | -                   | 9     |
| 9     | Ferulaldehyde                   | 7             | 1   | -        | -           | -     | -         | -        | -       | -        | 1                      | -                   | -                   | 9     |
| 10    | Isothymonin                     | 7             | -   | 1        | -           | 1     | 1         | -        | -       | 1        | 2                      | -                   | -                   | 13    |
| 11    | Isothymusin                     | 9             | -   | 1        | -           | -     | -         | -        | -       | -        | 2                      | 1                   | -                   | 13    |
| 12    | Linalool                        | 6             | 1   | -        | 1           | -     | -         | -        | -       | -        | 1                      | -                   | -                   | 10    |
| 13    | Luteolin                        | 11            | -   | -        | 1           | -     | -         | -        | -       | -        | 1                      | -                   | -                   | 13    |
| 14    | Ocimarin                        | 7             | -   | 1        | 1           | -     | -         | 1        | -       | -        | 2                      | -                   | 1                   | 13    |
| 15    | Rosmarinic acid                 | 8             | -   | 1        | -           | -     | -         | -        | -       | 1        | 6                      | -                   | -                   | 17    |
| 16    | Thymol                          | 4             | 3   | -        | 1           | -     | -         | 1        | -       | -        | 1                      | -                   | -                   | 10    |
| 17    | Saquinavir*                     | 12            | 1   | -        | 1           | 1     | 1         | 1        | -       | -        | 4                      | -                   | -                   | 20    |
| Total |                                 | 116           | 13  | 13       | 12          | 2     | 0         | 3        | 38      | 1        | 2                    | 206                 |                     |       |

*Positive Control - Synthetic HIV drug (Megha Hastantram Sampangi-Ramaiah et al., 2020)
Table 3: The 16 ligands of *Ocimum tenuiflorum* and the details of different bonds formed with 6Y2E protease of SARS-CoV2

| S. No | Ligand                                      | Van der Waals | C – H | Alkyl | Hydrogen | Pi-Alkyl | Pi-Hydrogen | Pi-Cation | Pi-Sigma | Pi-Stacked | Pi-Pi T shaped | Conventional | U-Ac | U-Do | Total |
|-------|---------------------------------------------|---------------|-------|-------|----------|----------|-------------|-----------|----------|------------|----------------|--------------|------|------|-------|
| 1     | (E)-6-hydroxy-4,6-dimethylhept-3-en-2-one   | 9             | 1     | -     | -        | -        | -           | -         | -        | -          | 2              | -             | -    | -    | 12    |
| 2     | Apigenin                                    | 7             | -     | 2     | 1        | -        | 1           | -         | 1        | -          | 1              | -             | -    | -    | 12    |
| 3     | Bieugenol                                   | 8             | 1     | 1     | 2        | -        | -           | -         | -        | -          | -              | 1             | -    | -    | 13    |
| 4     | Cirsilineol                                 | 7             | 3     | 1     | -        | -        | 1           | 1         | -        | -          | 1              | -             | 1    | -    | 13    |
| 5     | Cirsimaritin                                | 12            | 1     | 1     | 2        | -        | -           | -         | -        | -          | -              | -             | 16   |      |       |
| 6     | β-Caryophyllene epoxide                     | 9             | 1     | 1     | -        | -        | -           | -         | -        | -          | -              | -             | 11   |      |       |
| 7     | Dehydrodieugenol B                          | 8             | 1     | 1     | 3        | -        | 1           | -         | -        | 1          | -              | -             | 15   |      |       |
| 8     | Eugenol                                     | 7             | -     | -     | 1        | -        | -           | -         | 1        | -          | 2              | -             | 11   |      |       |
| 9     | Ferulatehyde                                | 6             | -     | 1     | -        | -        | -           | -         | -        | 1          | 3              | -             | 11   |      |       |
| 10    | Isothymonin                                 | 12            | 1     | 1     | -        | 1        | 1           | -         | -        | 1          | -              | -             | 16   |      |       |
| 11    | Isothymusin                                 | 11            | -     | -     | 1        | -        | -           | 1         | -        | -          | 1              | -             | 14   |      |       |
| 12    | Linalool                                    | 9             | -     | -     | 1        | -        | -           | -         | 1        | -          | 1              | -             | 11   |      |       |
| 13    | Luteolin                                    | 14            | -     | -     | 1        | -        | -           | -         | -        | 2          | 1              | -             | 18   |      |       |
| 14    | Ocimarin                                    | 11            | -     | -     | -        | 1        | -           | -         | -        | -          | 4              | -             | 15   |      |       |
| 15    | Rosmarinic acid                             | 14            | -     | -     | 2        | -        | -           | -         | -        | -          | 3              | 1             | 20   |      |       |
| 16    | Thymol                                      | 8             | -     | -     | -        | -        | -           | -         | -        | 1          | 1              | -             | 10   |      |       |
| 17    | Saquinavir*                                 | 10            | -     | -     | 4        | -        | 1           | -         | -        | -          | 3              | -             | 18   |      |       |
| Total |                                             | 162           | 8     | 8     | 18       | 4        | 1           | 2         | 1        | 3          | 27             | 1             | 1    | 236  |       |

*Positive Control - Synthetic HIV drug (Megha Hastantram Sampangi-Ramaiah et al., 2020)
bond (ASP 153 had one conventional hydrogen bond and one carbon hydrogen bond), one Pi-alkyl bond, one Pi-Pi stacked bond, eight van der Waals bonds for 6LU7 protease; it formed three conventional hydrogen bonds, two Pi-alkyl bonds, one unfavourable donor – donor bond and 14 van der Waals bonds (Figure 9).

CONCLUSION

As the binding affinity of Saquinavir (Sampangi-Ramaiah et al., 2020), the synthetic control drug, with 6LU7 protease showed 12 van der Waals, one alkyl, one Pi-alkyl, on Pi-cation, one Pi-stacked, four conventional hydrogen bonds, which indicates that it has less affinity when compared with Rosmarinic acid. Similarly, the synthetic control drug on binding with 6Y2E protease exhibited 10 van der Waals, four Pi-alkyl, one cation, three hydrogen bonds. The results are in conformity to similar other studies and herald a promising scope for Rosmarinic acid as lead molecule in the drug discovery for COVID-19.

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