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**ORIGINAL ARTICLE / ÖZGÜN MAKALE**

# MOLECULAR DOCKING STRATEGY FOR MULTI-TARGET INHIBITOR DISCOVERY OF SELECTED PLANT CONSTITUENTS IN *BAUHINIA ACUMINATA*

## *BAUHINIA ACUMINATA'DAKİ SEÇİLMİŞ FİTO BİLEŞENLERİN ÇOK HEDEFLİ İNHİBİTÖR KEŞFİ İÇİN MOLEKÜLER YERLEŞTİRME STRATEJİSİ*

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## ABSTRACT

**Objective:** *Traditional medicine is often considered to be a kind of complementary or alternative medicine (CAM) nowadays. Therefore, documenting and identifying the herbs that are effective in treating various diseases is vital for future disease control programs. This study aims to perform a molecular docking analysis of the thirteen plant components in Bauhinia acuminata against the target proteins in lung cancer (PDB IDs: 2ITY), breast cancer (1A52), diabetes (3L4U), obesity (IT02), inflammation (5COX) and corona viral infections (6VYO).*

**Material and Method:** *All the plant components used for the present study were retrieved from the plant Bauhinia acuminata and were evaluated for their biological activity results using molinspiration. Further in-silico docking analysis was performed using AutoDock Vina software and the binding interactions were visualized using Discovery studio program.*

**Result and Discussion:** *The docking scores and analysis of the interactions of the plant components with targets suggest that all the selected plant components showed excellent binding to the chosen targets when compared to that of the standard drugs. As a result of the docking process on 6 different targets, the selected plant components like Quercetin, Beta-sitosterol, and Rheagenine were observed to show good binding energy values against all the 5 targets except 6VYO as shown in (Table 9). These results can further pave the way for getting better insights in identifying and designing potential lead candidates.*

**Keywords:** *AutoDock Vina, Bauhinia acuminata, discovery studio, molecular docking, plant components*

## ÖZ

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**Amaç:** *Günümüzde geleneksel tıp genellikle bir tür tamamlayıcı veya alternatif tıp (CAM) olarak kabul edilmektedir. Bu nedenle, çeşitli hastalıkların tedavisinde etkili olan bitkilerin belgelenmesi ve tanımlanması gelecekteki hastalık kontrol programları için hayati öneme sahiptir. Bu çalışma Bauhiniaacuminata'daki on üç bitki bileşeninin akciğer kanseri (PDB IDs: 2ITY), meme kanseri (1A52), diyabet (3L4U), obezite (IT02), inflamasyon (5COX) ve korona viral enfeksiyonlarındaki (6VYO) hedef proteinlere karşı moleküler kenetlenme analizini gerçekleştirmeyi amaçlamaktadır.*

**Gereç ve Yöntem:** *Bu çalışmada kullanılan tüm bitki bileşenleri Bauhiniaacuminata bitkisinden alınmış ve molinspirasyon kullanılarak biyolojik aktivite sonuçları açısından değerlendirilmiştir. Ayrıca AutoDockVına yazılımı kullanılarak siliko içi yerleştirme analizi yapıldı ve bağlanma etkileşimleri Discoverystudio programı kullanılarak görselleştirildi.*

**Sonuç ve Tartışma:** *Yerleştirme puanları ve bitki bileşenlerinin hedeflerle etkileşimlerinin analizi, seçilen tüm bitki bileşenlerinin standart ilaçlarınkine kıyasla seçilen hedeflere mükemmel bağlanma gösterdiğini göstermektedir. 6 Farklı hedefe kenetlenme işlemi sonucunda, Quercetin, Beta-sitosterol ve Rheagenin gibi seçilen bitki bileşenlerinin, gösterildiği gibi 6VYO hariç tüm 5 hedefe karşı iyi bağlanma enerjisi değerleri gösterdiği gözlenmiştir (Tablo 9). Bu sonuçlar potansiyel potansiyel adayları belirleme ve tasarlama konusunda daha iyi kavrayışlar elde etmenin önünü daha da açabilir.*

**Anahtar Kelimeler:** *AutoDock Vina, Bauhinia acuminata, bitki bileşenleri, discovery studio, moleküler yerleştirme*

## INTRODUCTION

The World Health Organization (WHO) defines traditional medicine as: "the sum of total knowledge, practices, and skills based on the historical theories, beliefs, and experiences in indigenous to various cultures that are used to maintain the human or animal health and to prevent, diagnose, improve, or treat physical/mental illnesses" [1].

Herbal remedies are widely used in both developing and developed world countries to treat various illnesses indispensable [2]. The WHO reported, to treat their illnesses about 80% of the world's population are depending primarily on traditional medicines. Traditional medicine is often considered to be a kind of complementary or alternative medicine (CAM) [3] nowadays. Herbal medicines include herbal preparations, raw herbs, and finished herbal products, as well as additives derived from different kinds of plant parts/herbs. Many advantages are shown by the active components of these herbs, like lower toxicity and allergenicity than when compared to some commercial medications, regulating immunological responses, and causing viral destruction [4]. In the research trials [5], various common herbs have been used to prevent viral infections, and their efficacy has been demonstrated. Therefore, documenting and identifying the herbs that are effective in treating various contagious diseases is vital for future disease control programs.

*Bauhinia acuminata* is an ever green shrub belonging to the family of Fabaceae grown in the areas of South east Asia such as Malaysia, Indonesia, or the Philippines. For conventional drugs, bark, leaves, stem, blooms, and roots have been utilized. In India, it is a traditional plant, and its extract in studies have shown that *Bauhinia acuminata* have significant biological activities such as in the treatment of lung cancer [6], breast cancer [7], anti-diabetic [8], anti-obesity [9], anti-inflammatory [10]. Based on

the reported anti-lung cancer, anti-breast, anti-diabetic, anti-obesity activities, molecular docking studies have been planned to establish the contribution of the activity by the plant components.

*Bauhinia acuminata* has been chemically studied and reported wherein the important chemical constituents isolated from *Bauhinia acuminata* which are depicted in (Table 1) are chosen for our studies. All the plant components will be evaluated in this study on the docking behavior of EGFR [11], ESTROGEN ALPHA RECEPTOR [12], ALPHA GLUCOSIDASE [13], HMG COA [14], 5COX [15], SAR COV-2 [16] using an *In silico* molecular docking analysis with AutoDock Vina software and also an investigation on the enzymes binding sites using Discovery Studio Version 3.5.

## MATERIAL AND METHOD

The X-ray crystallographic structures of six different targets 2ITY (Lung cancer), 1A52 (Breast cancer), 3L4U (Diabetes), IT02 (Obesity), 5COX (Inflammation), 6VYO (Corona Virus infection) were retrieved from protein databank and saved as a Brookhaven protein data bank file [17]. For all the six targets, the standard ligands were selected from the literature review and downloaded from Pubchem Database as depicted in (Figure 1). The 2D structures of all thirteen plant components were sketched using ACD/Chemsketch Software as shown in (Table 1). The generated ligands were cleaned and performed 3D optimization and then saved in the MDL Molfile format. The ligands were then converted to a PDB file format using the Open Babel chemistry toolbox. AutoDock Vina [18] (Academic version.1.2.0, Molecular Graphics Lab (now CCSB) at The Scripps Research Institute) was used for molecular docking studies. A grid was generated around the co-crystallized ligand. The coordinates were generated with the help of MGL Tools and Pharmit: interactive exploration of chemical space [19]. Prepared pdbqt files for both target and ligands by adding Polar hydrogens and Gasteiger charges. Created in-house batch file of ligands and target and then docking was performed in the absence of water molecules for all the plant components [20]. The molecules were then analyzed after docking and visualized in the Discovery Studio Version 3.5 [21] for the interactions with the active site amino acids. Further to optimize the docking process all the crystal structures of the targets compared with the standard ligands. Ligand interactions were shown in (Figure 1 to Figure 6).

## RESULT AND DISCUSSION

Bioactivity score is a computational approach that can be used to determine whether or not a particular molecule is similar to the known drugs in its structural features and molecular properties. According to the bioactivity score, if >0 is active; if (−5.0 to − 0.0) is moderately active, and if <−5.0 is inactive. In the present study, all the thirteen plant components of *Bauhinia acuminata* showed active scores (>0) toward enzyme inhibitors descriptors. However, for other descriptors, these compounds

exhibited active to moderate active scores with none showing inactive score (<−5.0), as shown in (Table 2) which is already reported and is considered for our present work [22].

**Table 1.** Names and structures of the plant constituents of *Bauhina acuminata*

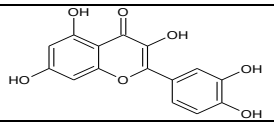
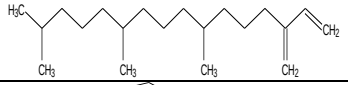
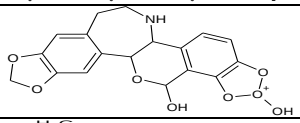
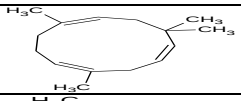
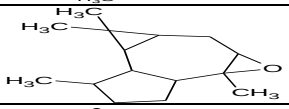
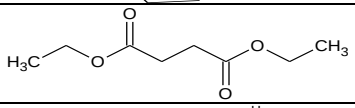
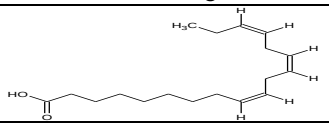
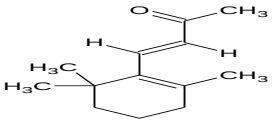
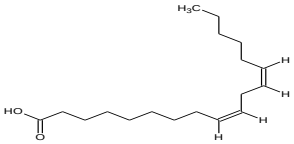
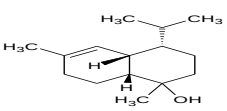
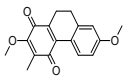
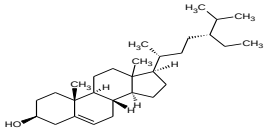
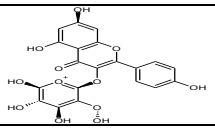
| S.No | Plantconstituent | Structure |
|---|---|---|
| **1** | Quercetin |  |
| **2** | Neophytadiene |  |
| **3** | Rheagenine |  |
| **4** | Alpha humulene |  |
| **5** | Isoaromadendrene epoxide |  |
| **6** | Butanedioic acid diethyl ester |  |
| **7** | 9,12,15-octadecatrienoic acid |  |
| **8** | Beta-ionone |  |
| **9** | 9,12-octadecadienoic acid |  |
| **10** | Alpha muurolol |  |
| **11** | Bauhinione |  |
| **12** | Beta-sitosterol |  |
| **13** | Kaempferol-3-glucoside |  |

**Table 2.** Computed biological activity results of the plant constituents of *Bauhinia acuminata* by molinspiration

| S.No | Plant Constituent | GPCR Ligand | Ion Channel Modulator | Kinase Inhibitor | Nuclear Receptor Ligand | Protease Inhibitor | Enzyme Inhibitor |
|---|---|---|---|---|---|---|---|
| **1** | Quercetin | -0.06 | -0.19 | 0.28 | 0.36 | -0.25 | 0.28 |
| **2** | Neophytadiene | -0.12 | -0.02 | -0.35 | 0.2 | -0.11 | 0.14 |
| **3** | Rheagenine | 0.21 | 0.13 | -0.14 | -0.09 | 0.02 | 0.17 |
| **4** | Alpha humulene | -0.14 | 0.02 | -0.93 | 0.34 | -0.67 | 0.31 |
| **5** | Isoaromadendrenee poxide | -0.39 | -0.37 | -0.69 | -0.01 | 0.02 | -0.05 |
| **6** | Butanedioicaciddiet hyl ester | -0.93 | -0.35 | -1.19 | -0.91 | -0.92 | -0.46 |
| **7** | 9,12,15-octadecatrienoic acid | 0.29 | 0.17 | -0.16 | 0.31 | 0.12 | 0.38 |
| **8** | Beta-ionone | -0.9 | -0.26 | -1.34 | 0.25 | -0.79 | 0.28 |
| **9** | 9,12-octadecadienoic acid | 0.29 | 0.17 | -0.16 | 0.31 | 0.12 | 0.38 |
| **10** | Alpha muurolol | -0.09 | 0.05 | -0.87 | 0.39 | -0.63 | 0.4 |
| **11** | Bauhinione | -0.13 | -0.18 | 0.1 | 0.06 | -0.29 | 0.34 |
| **12** | Beta-sitosterol | 0.14 | 0.04 | -0.51 | 0.73 | 0.07 | 0.51 |
| **13** | Kaempferol-3-glucoside | 0.06 | -0.05 | 0.1 | 0.2 | -0.05 | 0.41 |

In this *in silico* study, we have seen that thirteen plant components of *Bauhinia acuminata* exhibited the most negative value of docking score toward 2ITY, 1A52, 3L4U, IT02, 5COX means the best affinity was formed except for 6VYO. The docking scores and analysis of the interactions of the plant components with targets suggest that all the selected plant components showed excellent binding to the chosen targets when compared to that of the standard drugs.

Molecular docking interactions of all plant components with the target 1A52 were elucidated, and it was observed that various hydrogen bond interactions with aminoacids LEUA:387, ILEA:424, META:421, HISA:524, GLYA:521, GLUA:353, ARGA:394, ARGA:434, LEUA:384, META:388, META:343, THRA:347, LEUA:349, LEUA:354, LEUA:428, META:388, TRPA:383, ARGA:515, GLUA:323, TRPA:393 were determined. Binding energies of all the compounds were found between -5.6 to -8.6 kcal/mol which were illustrated in (Table 3). All the plant components except Butanedioic acid diethyl ester showed more binding energies than the standard Tamoxifen (-6.2 kcal/mol).

All the plant components when docked with target 2ITY the following hydrogen bond interactions with aminoacids LEUA:844, PROA:794, LYSA:745, META:793, LYSA:745, LEUA:718, VALA:726, ASPA:855, GLYA:719, LEUA:844, GLNA:791, GLUA:762, THRA:854, SERA:720, ASPA:855 were determined. Binding energies of all the compounds were found between -5.1 to -9.2 kcal/mol which were illustrated in (Table 4). Among all compounds, Rheagenine, Beta-sitosterol, Bauhinione, Quercetin, Kaempferol-3-glucoside, and Isoaromadendrene epoxide showed more binding energies than the standard Erlotinib ( -7.1 kcal/mol).

**Table 3.** Calculated binding energy values and interaction properties of the plant constituents of the phyto-constituents of *Bauhinia acuminata* the target 2ITY

| S.No | Plant constituent | Binding Energy (kcal/mol) | Hydrogen Bond Interactions | Alkyl/π Alkyl Interactions |
|---|---|---|---|---|
| **1** | Quercetin | -8 | META:793, GLNA:791, ASPA:855, GLUA:762 | LEUA:844, LEUA:718, ALAA:743, LYSA:745, VALA:726 |
| **2** | Neophytadiene | -5.3 | META:793 | LEUA:844, LEUA:718, ALAA:743, VALA:726 |
| **3** | Rheagenine | -9.2 | LEUA:844, META:793 | ALAA:743, VALA:726 |
| **4** | Alpha humulene | -6.7 | LEUA:718 | VALA:726 |
| **5** | Isoaromadendreneepoxide | -7.4 | No Interactions | LEUA:858, LEUA:747, PHEA:723 |
| **6** | Butanedioicaciddiethyl ester | -5.5 | GLYA:719, SERA:720, PHEA:723, THRA:725, LYSA:745, ASPA:855 | LEUA:718, VALA:726, CYSA:797 |
| **7** | 9,12,15-octadecatrienoic acid | -5.6 | ASPA:855 | VALA:726, LEUA:844, LEUA:718, LEUA:792, ALAA:743, META:793 |
| **8** | Beta-ionone | -6.4 | VALA:726, LEUA:844, META:793 | No Interactions |
| **9** | 9,12-octadecadienoic acid | -5.1 | LYSA:745, ASPA:855, THRA:854 | LEUA:844, LEUA:718, ALAA:743, VALA:726 |
| **10** | Alpha muurolol | -6.8 | No Interactions | LEUA:844, CYSA:775, LEUA:718, LEUA:792, ALAA:743, VALA:726 |
| **11** | Bauhinione | -8.1 | LYSA:745, ASPA:855 | ALAA:743, LEUA:844, LEUA:718, VALA:726 |
| **12** | Beta-sitosterol | -8.4 | PROA:794, LEUA:844 | ALAA:743, LEUA:718, VALA:726 |
| **13** | Kaempferol-3-glucoside | -7.9 | META:793, GLUA:762 | LEUA:844, LEUA:718, ALAA:743, VALA:726, LYSA:745 |
| **14** | ERLOTINIB (STANDARD) | -7.1 | LYSA:745, THRA:854, GLYA:721, GLYA:719 | ALAA:743, LEUA:844, LEUA:718, VALA:726 |

All the plant components when docked with target 3L4U target the following hydrogen bond interactions with amino acids ASPA:203, THRA:204, LYSA:480, THRA:205, GLUA:333, TYRA:299, HISA:600, ASPA:203, THRA:205, GLNA:603, ASPA:203, GLUA:404, ASPA:542, ARGA:526, ARGA:542, THRA:205, LYSA:480, PHEA:450, GLUA:404, ASPA:443. Binding energies of all the compounds were found between -5.3 to -8.3 kcal/mol which were illustrated in (Table 5). Among all compounds Rheagenine, Beta-sitosterol and Quercetin showed more binding energies than the standard Acarbose (-7.1 kcal/mol).

All the plant components made hydrogen bond interactions with aminoacids ASNB:375, GLYA:536, TYRB:373, ASNA:375, ASNB:375, PHEB:142, GLYB:225, GLNA:241, PROB:538, LYSA:333, GLYA:227, HISB:226, ASNA:375, GLNB:374, VALB:228, ARGB:376, TRPB:139, GLNA:241, ARGB:376, ARGA:376, GLYA:225, LYSA:333, GLUB:140, LEUB:145, ASNB:144, LEUA:145, TYRA:373 in the active site of 5COX target. Binding energies of all the compounds were found between -5 to -9.9 kcal/mol which were illustrated in (Table 6). Among all compounds, Rheagenine, Beta-sitosterol, Bauhinione, Quercetin, Kaempferol-3-glucoside, Iso aromadendrene

epoxide, alpha Muurolol, Alpha Humulene, Beta-Ionone, and Butanedioic acid diethyl ester showed more binding energies than the standard Aspirin (-5.8 kcal/mol).

**Table 4.** Calculated binding energy values and interaction properties of the plant constituents of *Bauhinia acuminata* the target 1A52

| S. No | Plant Constituent | Binding energy (kcal/mol) | Hydrogen Bond Interactions | Alkyl/π Alkyl Interactions |
|---|---|---|---|---|
| **1** | Quercetin | -8.5 | GLYA:521, GLUA:353, ARGA:394 | META:421, ILEA:424, LEUA:391, ALAA:350, LEUA:387, PHEA:404, LEUA:384 |
| **2** | Neophytadiene | -6.8 | LEUA:428, META:388, TRPA:383 | LEUA:525, LEUA:387, LEUA:391, PHEA:404, ALAA:350, LEUA:384 |
| **3** | Rheagenine | -7.2 | No Interactions | LEUA:354, TRPA:383, ASPA:351 |
| **4** | Alpha humulene | -8 | LEUA:384, META:388 | No Interactions |
| **5** | Isoaromadendreneepoxide | -8.3 | ARGA:434 | LEUA:509, HISA:513, ILEA:510, PHEA:404, LEUA:384 |
| **6** | Butanedioicaciddiethyl ester | -5.6 | GLUA:323, TRPA:393 | LEUA:403, ARGA:394, META:396, PROA:324, ILEA:326 |
| **7** | 9,12,15-octadecatrienoic acid | -7 | HISA:524, GLYA:521 | LEUA:346, PHEA:404, META:388, LEUA:391, LEUA:387, ALAA:350, LEUA:384, LEUA:525, TRPA:383 |
| **8** | Beta-ionone | -7.2 | THRA:347 | ALAA:350, LEUA:387, PHEA:404, LEUA:391 |
| **9** | 9,12-octadecadienoic acid | -6.8 | ARGA:394, LEUA:387 | TRPA:383, ALAA:350, LEUA:384, LEUA:525, PHEA:404, ILEA:424, META:421, LEUA:391, META:388, LEUA:346 |
| **10** | Alpha muurolol | -7.9 | META:343, THRA:347, LEUA:349 | ALAA:350, LEUA:387, PHEA:404, LEUA:525, LEUA:384, TRPA:383, LEUA:346, META:421 |
| **11** | Bauhinione | -8.6 | LEUA:387, ILEA:424, META:421, HISA:524 | LEUA:346, ALAA:350, PHEA:404 |
| **12** | Beta-sitosterol | -7 | LEUA:354 | VALA:376, ILEA:358, LEUA:372, TRPA:383 |
| **13** | Kaempferol-3-glucoside | -8.4 | ARGA:394, GLUA:353 | ILEA:424, META:421, LEUA:387, ALAA:350, LEUA:391 |
| **14** | TAMOXIFEN (STANDARD) | -6.2 | ARGA:515 | LEUA:508,LEUA:479, ILEA:451 |

Molecular docking interactions of the plant components were elucidated with 6VYO target, were various hydrogen bond interactions like ALAA:50, TYRA:111, ARGA:88, TYRA:109, ALAA:55, ARGA:107, ASNB:153, VALA:158, ILEB:157, ILEB:146, THRB:76, ASNB:77, ALAA:55, ARGA:107, ASNB:75, SERA:105, SERB:79, THRB:141, HISA:59, ASPB:81 were observed. Binding energies of all the compounds were found between -5.7 to -9.7 kcal/mol which were illustrated in (Table 7). Among all compounds, Isoaromadendreneepoxide showed more binding energy than the standard N3 inhibitor of 6LU7 (-5.8 kcal/mol).

**Table 5.** Calculated binding energy values and interaction properties of the plant constituents of *Bauhinia acuminata* the target 3L4U

| S.No | Plant Constituent | Bindin genergy (kcal/mol) | Hydrogen Bond Interactions | Alkyl/π Alkyl Interactions |
|---|---|---|---|---|
| **1** | Quercetin | -7.3 | ASPA:542 | ASPA:443, META:444, PHEA:575, TYRA:299, TRPA:406 |
| **2** | Neophytadiene | -5.7 | TYRA:299 | TRPA:441, HISA:600, PHEA:575, TRPA:406, PHEA:450 |
| **3** | Rheagenine | -8.3 | ASPA:203 | LYSA:480, ASPA:542. TRPA:406 |
| **4** | Alpha humulene | -6 | No Interactions | PHEA:575, ALAA:576 |
| **5** | Isoaromadendrene epoxide | -5.8 | GLUA:333 | ARGA:334 |
| **6** | Butanedioic acid diethyl ester | -5.9 | THRA:205, ASPA:203, THRA:204 | ILEA:328, TRPA:406, TYRA:605, PHEA:575, ALAA:576, TYRA:299 |
| **7** | 9,12,15-octadecatrienoic acid | -5.5 | HISA:600 | TYRA:299, PHEA:575, ALAA:576, TYRA:605, ASPA:443 |
| **8** | Beta-ionone | -5.3 | GLNA:603 | TRPA:406 |
| **9** | 9,12-octadecadienoic acid | -5.4 | THRA:205 | LYSA:480, TRPA:406, PHEA:575, PHEA:450, ILEA:328, TYRA:299 |
| **10** | Alpha muurolol | -5.4 | ASPA:203 | PHEA:450, LYSA:480 |
| **11** | Bauhinione | -6.4 | LYSA:480, PHEA:450, GLUA:404 | No Interactions |
| **12** | Beta-sitosterol | -7.5 | GLUA:404 | PHEA:575, PHEA:450 |
| **13** | Kaempferol-3-glucoside | -7.1 | ARGA:526, ASPA:542, ASPA:443 | TYRA:299, PHEA:575, TRPA:406 |
| **14** | ACARBOSE (STANDARD) | -7.1 | No Interactions | TYRA:301, GLUA:333, ASPA:340, GLUA:300, ASPA:329, GLYA:302 |

All the plant components made hydrogen bond interactions with aminoacids PHEA:10, ALAA:63, ARGA:18, PROA:61, SERA:66, ARGA:18, VALA:64, VALA:87, ALAA:88, ARGA:11, PROA:275, VALA:81, TYRA:62, ASNA:67, SERA:91, PROA:84 in the active site of 1T02 target. Binding energies of all the compounds were found between -6.32 to -8.7 kcal/mol were illustrated in (Table 8). Among all compounds, Rheagenine, Beta-sitosterol, Bauhinione, Quercetin showed more binding energies than the Standard Simvastatin (-7.7 kcal/mol).

As a result of the docking process on 6 different targets, the selected plant components like Quercetin, Beta-sitosterol, and Rheagenine were observed to show better binding energy values against all the 5 targets except 6VYO as shown in (Table 9).

This present study has paved the way in understanding that some of the plant components of *Bauhinia acuminata* may act as potential inhibitors against enzyme targets namely 2ITY, 1A52, 3L4U, IT02, 5-COX except 6VYO.

As a result of the docking process on 6 different targets, the selected plant components like Quercetin, Beta-sitosterol, and RHEAGENINE were observed to show good binding energy values against all the 5 targets except 6VYO. This research can further provide better insights in identifying and designing potential lead candidates against Lung cancer, breast cancer, diabetes, obesity, and inflammation in the area of drug discovery.

**Table 6.** Calculated binding energy values and interaction properties of the plant constituents of *Bauhinia acuminata* the target 1T02.

| S.No | Plant Constituent | Binding energy (kcal/mol) | Hydrogen Bond Interactions | Alkyl/π Alkyl Interactions |
|---|---|---|---|---|
| **1** | Quercetin | -7.8 | ASNA:67, SERA:91, ALAA:88 | VALA:87, ARGA:11 |
| **2** | Neophytadiene | -6.3 | No Interactions | VALA:64, ALAA:63, ARGA:18, LEUA:19, ILEA:22, LEUA:36, PHEA:10, PROA:15 |
| **3** | Rheagenine | -8.7 | SERA:66, ALAA:88, ARGA:18 | VALA:87, ALAA:63, PHEA:10, ARGA:11 |
| **4** | Alpha humulene | -7.1 | LEUA:19, ARGA:18 | No Interactions |
| **5** | Isoaromadendrene epoxide | -7.3 | PROA:275, VALA:81 | VALA:278, TRPA:284 |
| **6** | Butanedioic acid diethyl ester | -6.6 | ARGA:18, VALA:64 | VALA:87, ALAA:88, ARGA:11, LEUA:19, ILEA:22, ILEA:344, TYRA:62, LEUA:36, LEUA:19 |
| **7** | 9,12,15-octadecatrienoic acid | -6.7 | SERA:66, SERA:91, VALA:64 | VALA:87, PHEA:10, ALAA:63, PROA:15, ARGA:18, LEUA:19, ILEA:22, LEUA:36, TYRA:62 |
| **8** | Beta-ionone | -6.3 | ARGA:18 | ILEA:22, VALA:64, LEUA:19 |
| **9** | 9,12-octadecadienoic acid | -6.4 | SERA:66, SERA:91, VALA:87, ALAA:88, ARGA:11 | VALA:64, ALAA:63, ARGA:18, LEUA:19, ILEA:22, LEUA:36, PHEA:10 |
| **10** | Alpha muurolol | -7.6 | TYRA:62 | ILEA:344, VALA:64, LEUA:36, ILEA:22, LEUA:19, PROA:15, ARGA:18 |
| **11** | Bauhinione | -8 | ASNA:67, SERA:66, SERA:91, ARGA:11 | ALAA:88 |
| **12** | Beta-sitosterol | -8.3 | PROA:84 | PROA:61, ALAA:63, VALA:87, ARGA:11 |
| **13** | Kaempferol-3-glucoside | -7.6 | No Interactions | LEUA:19, ILEA:22, VALA:87 |
| **14** | SIMVASTATIN (STANDARD) | -7.7 | PHEA:10, ALAA:63, ARGA:18, PROA:61 | VALA:87 |

**Table 7.** Calculated binding energy values and interaction properties of the plant constituents of *Bauhinia acuminata* the target 5COX

| S.No | Plant Constituent | Binding energy (kcal/mol) | Hydrogen Bond Interactions | Alkyl/π Alkyl Interactions |
|---|---|---|---|---|
| **1** | Quercetin | -8.4 | TYRB:373, GLNB:374, ARGA:376, ASNA:375, TYRA:373 | PHEA:142 |
| **2** | Neophytadiene | -5 | LEUA:145 | PHEB:142, LEUB:145, PHEA:142 |
| **3** | Rheagenine | -9.9 | ASNB:375, ASNA:375, ARGB:376, LEUB:145, LEUA:145 | No Interactions |
| **4** | Alpha humulene | -6.5 | PHEB:142 | No Interactions |
| **5** | Isoaromadendrene epoxide | -7.1 | PHEB:142, ARGB:376, LEUA:145 | No Interactions |
| **6** | Butanedioic acid diethyl ester | -6.2 | PROB:538 | PHEA:142 |
| **7** | 9,12,15-octadecatrienoic acid | -5.2 | HISB:226 | LEUA:145, PHEA:142 |
| **8** | Beta-ionone | -6.2 | GLNA:241, TRPB:139, LYSA:333, GLUB:140 | LEUA:238 |
| **9** | 9,12-octadecadienoic acid | -5.4 | GLYA:227, ASNA:375 | LEUA:145, PHEB:142, LEUB:145 |
| **10** | Alpha muurolol | -6.7 | GLYB:225, ASNB:375 | HISB:226, LEUB:145, PHEA:142 |
| **11** | Bauhinione | -8.1 | ASNA:375, LEUA:145, GLYA:225 | PROA:538, PHEB:142 |
| **12** | Beta-sitosterol | -9.3 | GLYA:536 | PHEB:142 |
| **13** | Kaempferol-3-glucoside | -8.1 | ASNB:375, VALB:228 | PROB:538 |
| **14** | ASPRIN (STANDARD) | -5.8 | LYSA:333, GLNA:241, GLUB:140, ASNB:144 | No Interactions |

**Table 8.** Calculated binding energy values and interaction properties of the plant constituents of *Bauhinia acuminata* the target 6VYO

| S.No | Plant Constituent | Binding energy (kcal/mol) | Hydrogen Bond Interactions | Alkyl/π Alkyl Interactions |
|---|---|---|---|---|
| **1** | Quercetin | -8.1 | ASNB:153 | ARGA:107, TRPB:52, ALAA:55 |
| **2** | Neophytadiene | -5.7 | No Interactions | ILEB:74, ILEB:157, VALA:158, TRPB:52, CLA:202, ILEB:146 |
| **3** | Rheagenine | -7.9 | THRB:76, ASNB:77 | ILEB:157, VALA:158 |
| **4** | Alpha humulene | -8.7 | No Interactions | No Interactions |
| **5** | Isoaromadendrene epoxide | -9.7 | VALA:158, ILEB:157, ILEB:146 | TRPB:52 |

**Table 8 (*continued*).** Calculated binding energy values and interaction properties of the plant constituents of *Bauhinia acuminata* the target 6VYO.

| S.No | Plant Constituent | Binding energy (kcal/mol) | Hydrogen Bond Interactions | Alkyl/π Alkyl Interactions |
|---|---|---|---|---|
| 6 | Butanedioic acid diethyl ester | -6.7 | ALAA:55, ARGA:107, ARGA:149, ASNB:154, ASNB:153 | ILEB:157, ALAA:50, TYRA:109, VALA:158, TRPB:52 |
| 7 | 9,12,15-octadecatrienoic acid | -6.4 | ARGA:92, ARGA:107, THRB:148 | CLA:202, TRPB:52, ILEB:146 |
| 8 | Beta-ionone | -7.8 | ALAA:55,ARGA:107 | TRPB:52 |
| 9 | 9,12-octadecadienoic acid | -6.3 | ALAB:155, ALAA:156, ASNB:154 | ILEB:146, ILEB:157, CLA:202, ALAA:55, TYRA:109, TRPB:52 |
| 10 | Alpha muurolol | -7.8 | No Interactions | ILEB:157, VALA:158, TRPB:52, ALAA:55 |
| 11 | Bauhinione | -6.9 | SERA:105, SERB:79, THRB:141, HISA:59, ASPB:81 | HISB:145, ASPB:144, LYSA:102, PROB:142 |
| 12 | Beta-sitosterol | -7.2 | No Interactions | TYRA:172, PROB:80, PROB:162 |
| 13 | Kaempferol-3-glucoside | -7.6 | ALAA:55, ASNB:75 | ILEB:146, TRPB:52, ARGA:107 |
| 14 | N3 INHIBITOR of 6LU7 (STANDARD) | -8.7 | ALAA:50, TYRA:111, ARGA:88, TYRA:109, ALAA:55, ARGA:107, ASNB:153 | PROA:117, TRPB:52 |

**Table 9.** Binding energy values of prioritized plant constituents of *Bauhinia acuminata* againsts elected targets

| Target protein | 2ITY | 1A52 | 3L4U | IT02 | 5COX | 6VYO |
|---|---|---|---|---|---|---|
| **Plant constituent** | Binding energy (kcal/mol) | | | | | |
| **Quercetin** | -8 | -8.5 | -7.3 | -7.8 | -8.4 | -8.1 |
| **Beta sitosterol** | -8.4 | -7 | -7.5 | -8.3 | -9.3 | -7.2 |
| **Rheagenine** | -9.2 | -7.2 | -8.3 | -8.7 | -9.9 | -7.9 |
| **Standard** | -7.1 | -6.2 | -7.1 | -7.7 | -5.8 | -8.7 |

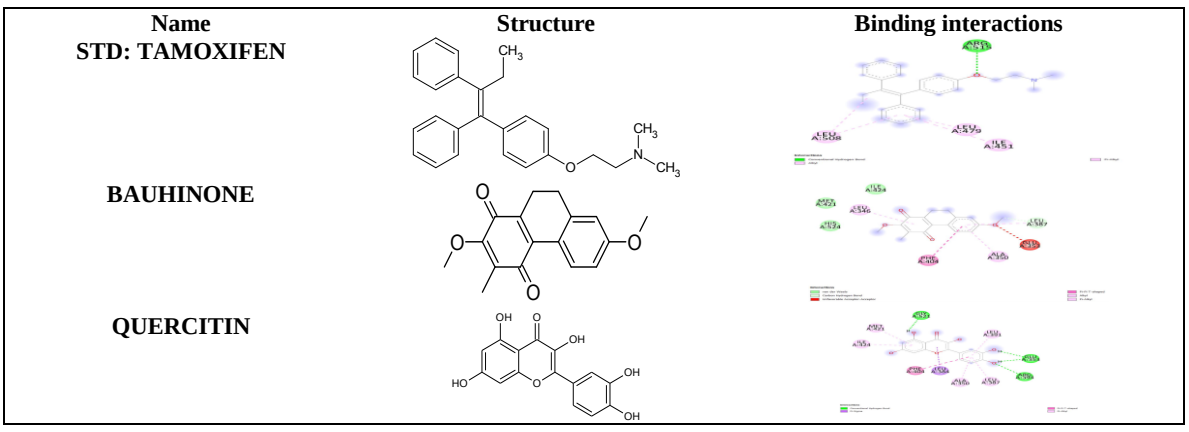



**Figure 1.** Docking interaction of Tamoxifen (Standard), Bauhinione and Quercetin within the active site of target 1A52

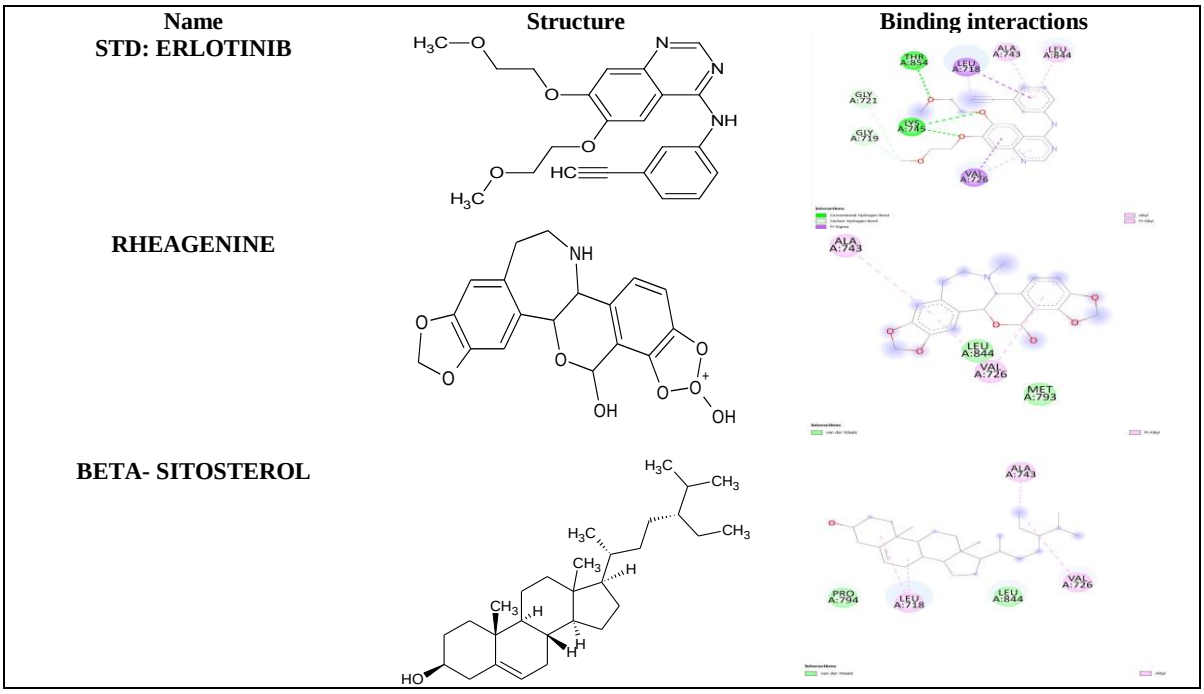



**Figure 2.** Docking interaction of Erlotinib (Standard), RHEAGENINE and Beta-sitosterol within the active site of target 2ITY

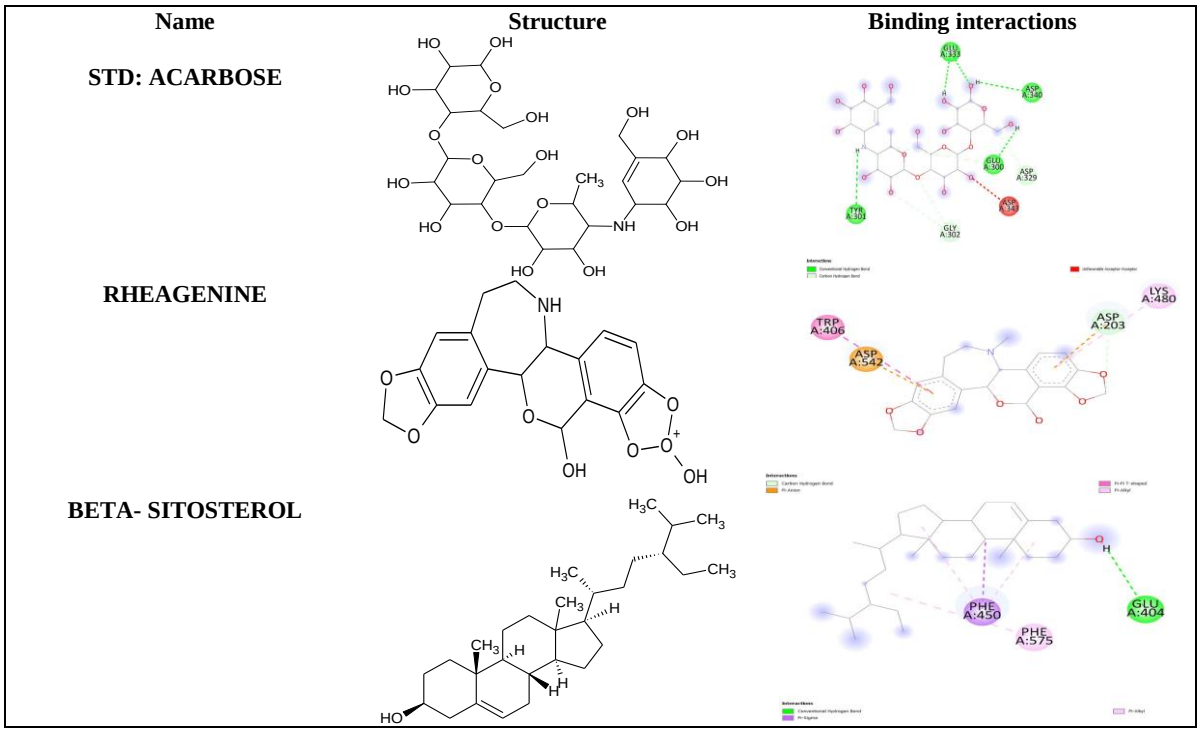



**Figure 3.** Docking interaction of Acarbose (Standard), RHEAGENINE and Beta-sitosterol within the active site of target 3L4U

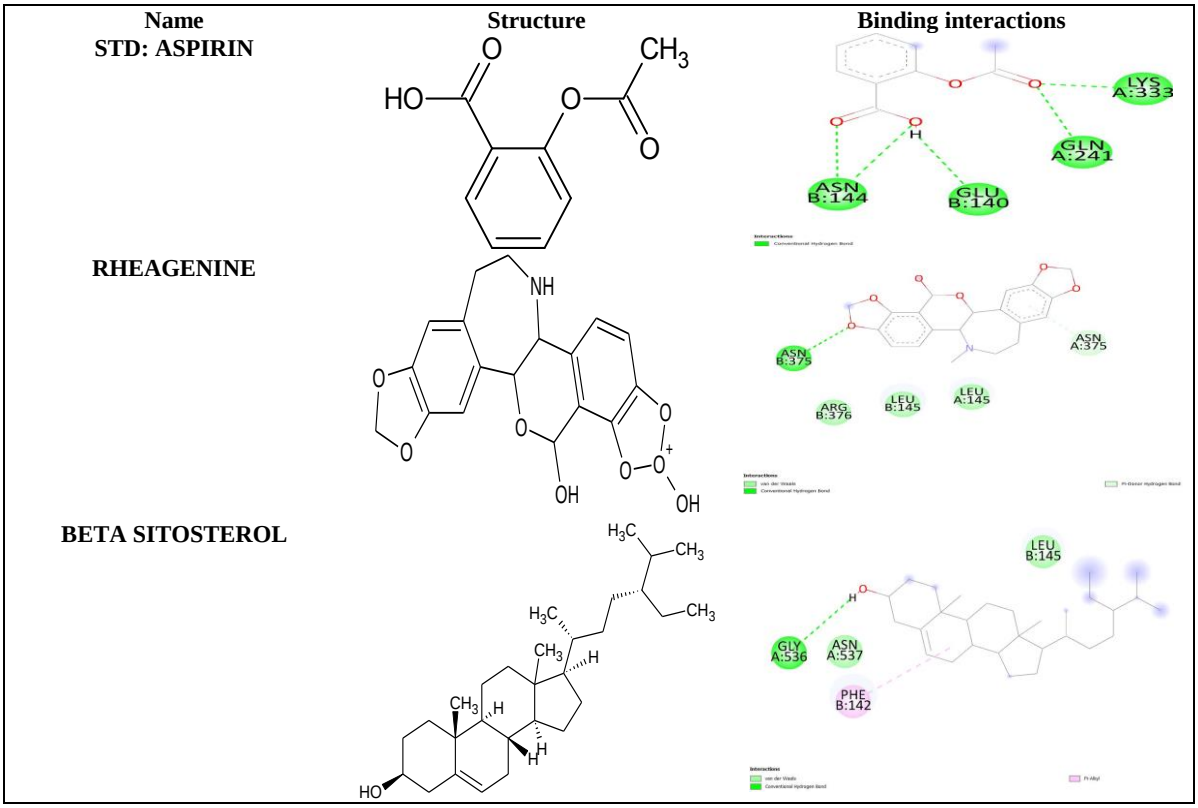



**Figure 4.** Docking interaction of Aspirin (Standard), RHEAGENINE and Beta-sitosterol within the active site of target 5COX

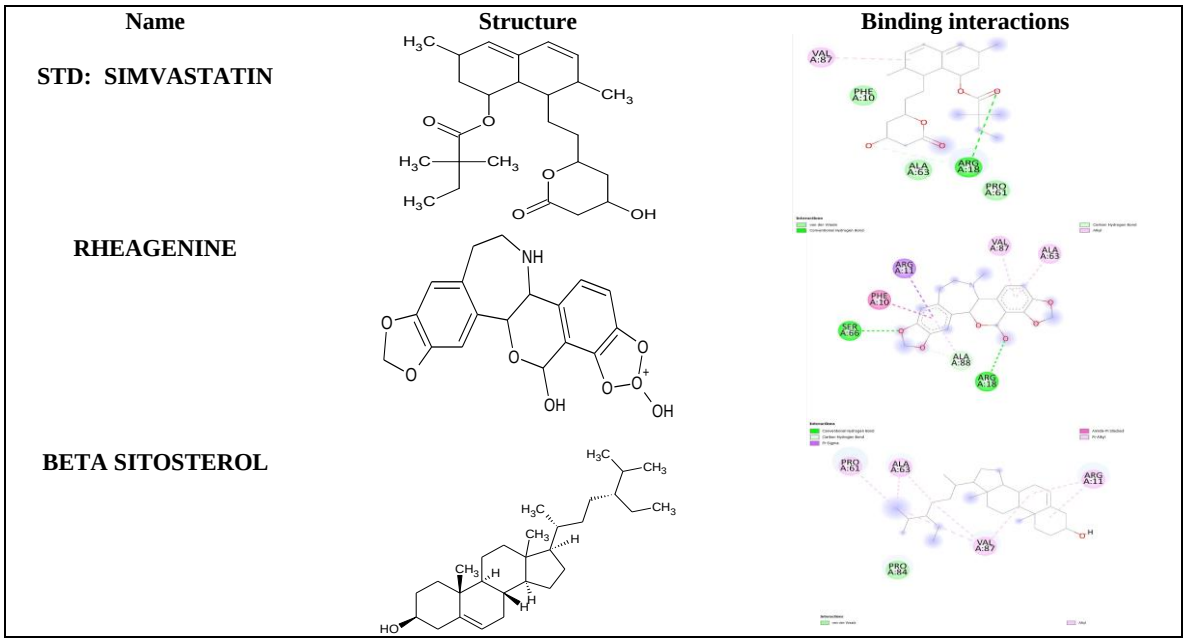



**Figure 5.** Docking interaction of Simvastatin (Standard), RHEAGENINE and Beta-sitosterol within the active site of target 1T02

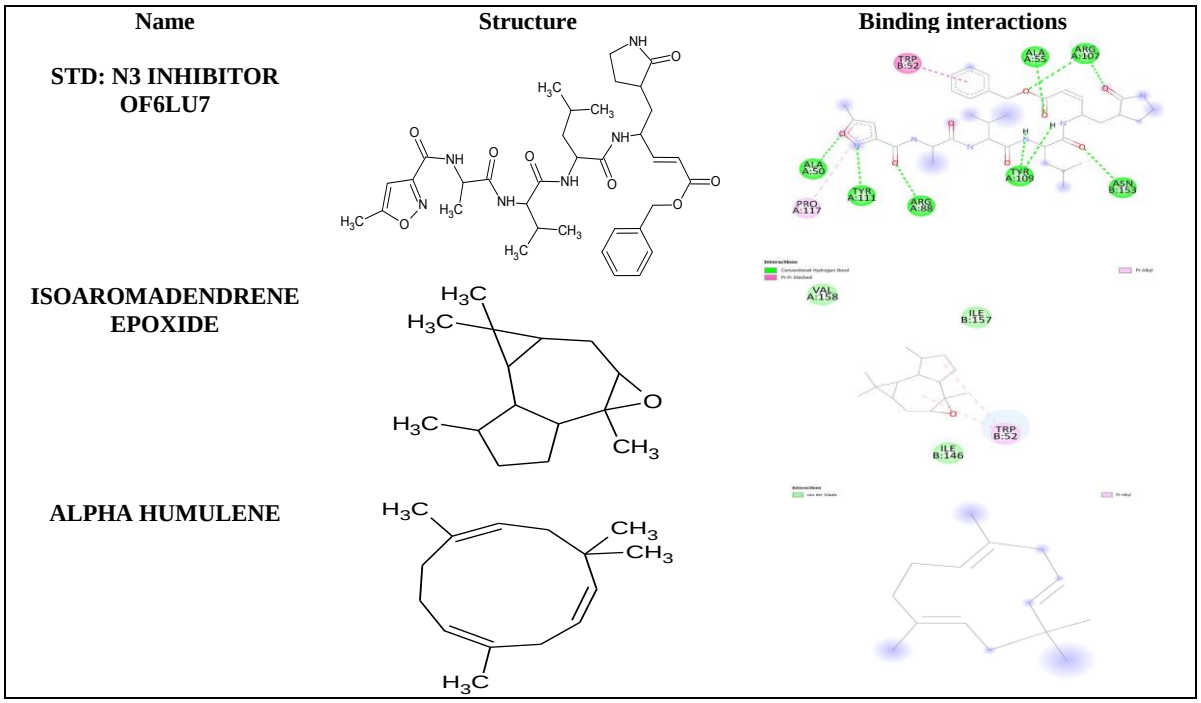



**Figure 6.** Docking interaction of N3 Inhibitor of 6LU7(Standard), Isoaromadendrene epoxide and Alpha Humulene within the active site of target 6VYO

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## AUTHOR CONTRIBUTIONS

Concept: *N.K.*; Design: *V.K., M.S.*; Supervision: *N.K.*; Resources: *V.K., M.S.*; Materials: *M.S., V.K.*; Data Collection and/or processing: *N.K., V.K., M.S.*; Analysis and/or interpretation: *N.K., M.S.*; Literaturereview: *N.K.*; Manuscript writing: *N.K., V.K., M.S.*; Critical review: *N.K., V.K, M.S.*

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ETHICS COMMITTEE APPROVAL

The authors declare that the ethics committee approval is not required for this study.

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