Scores of each of the antibiotics we tested

|  |  |  |
| --- | --- | --- |
| Ligand Name | CID | Binding Affinity |
| Ampicillin\_6249 | 6249 | -7.716 |
| Minocycline\_54675783 | 54675783 | -7.631 |
| Meropenem\_441130 | 441130 | -7.405 |
| Colistin\_44144393 | 44144393 | -7.575 |
| Doripenem\_73303 | 73303 | -8.065 |
| Imipenem\_104838 | 104838 | -6.83 |
| Cefotaxime\_5742673 | 5742673 | -7.373 |

Baseline for Top hits

Baseline for Moderate hits

Baseline for Bottom hits

All others were eliminated

**The code responsible for this can be found in the repository as python\_codefiles/post\_docking\_screening.py**

Please make table accordingly (Only Compounds that showed the highest docking score)

|  |  |
| --- | --- |
| Ligand Name | Binding Affinity (kcal/mol) |
| Asperglaucide\_**10026486** | -8.164 |
| Azadiradione\_**12308714** | -8.143 |
| beta-Sitosterol-beta-D-glucoside\_**12309055** | -8.7 |
| Procyanidin B5\_**124017** | -9.59 |
| Chelerythrine\_**2703** | -8.357 |
| Carnosol\_**442009** | -8.086 |
| Fenugreekine\_**444170** | -8.643 |
| Quercetin\_**5280343** | -8.214 |
| Stigmasterol\_**5280794** | -8.214 |
| Rutin\_**5280805** | -8.893 |
| Kaempferol\_**5280863** | -8.164 |
| Myricetin\_**5281672** | -8.234 |
| Afzelin\_**5316673** | -8.11 |
| Sophoraflavanone G\_**72936** | -8.695 |
| alpha-Amyrin\_**73170** | -8.163 |
| Corilagin\_**73568** | -8.816 |
| Taraxerol\_**92097** | -8.279 |

Next, we performed a plip analysis to assess all the residues each ligand was binding to, the configuration (**also found in the file python\_codefiles/post\_plip\_screening.py),** which decided which compounds to keep based on the research paper for our target protein:

# Key active-site or functional residues (resname + resnumber, e.g. ARG261)

KEY\_RESIDUES = {'SER81', 'TRP221', 'ARG261', 'TYR112', 'MET223', 'VAL130', 'LYS84'}

# Weights for different interaction types (base importance)

INTERACTION\_WEIGHTS = {

    "H\_pdon”: 3.0,

    "H\_ldon": 3.0,

    "Salt": 4.0,

    "Hydrophobic": 1.5,

    "Pi": 2.0,

    "Pication": 2.5

}

# Distance and angle thresholds for optimal hydrogen bonding

MIN\_DIST = 1.5

MAX\_DIST = 4.0

IDEAL\_ANGLE = 180

ANGLE\_TOL = 60

The key interactions and behaviors were also found for our baseline antibiotics and are seen below:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Ligand Name** | **CID** | **Binding Affinity** | **Interaction Score** | **Key Interactions** |
| Cefotaxime\_5742673 | 5742673 | -7.373 | 0.895 | ARG261 (H\_pdon, 2.41 Ã…, 105.2Â°); LYS84 (Salt, 5.09 Ã…); SER81 (H\_pdon, 2.02 Ã…, 134.3Â°); TRP221 (H\_pdon, 2.98 Ã…, 136.1Â°) |
| Imipenem\_104838 | 104838 | -6.83 | 1.008 | ARG261 (Salt, 3.99 Ã…); LYS84 (H\_pdon, 2.98 Ã…, 143.4Â°); SER81 (H\_pdon, 3.32 Ã…, 129.2Â°); TRP221 (H\_pdon, 2.18 Ã…, 129.7Â°); TYR112 (Hydrophobic, 3.94 Ã…) |
| Doripenem\_73303 | 73303 | -8.065 | 1.422 | ARG261 (H\_ldon, 2.40 Ã…, 130.1Â°); ARG261 (Salt, 4.23 Ã…); SER81 (H\_pdon, 2.97 Ã…, 122.1Â°); SER81 (H\_pdon, 3.38 Ã…, 130.1Â°); TRP221 (H\_pdon, 2.23 Ã…, 140.0Â°); TYR112 (Hydrophobic, 3.63 Ã…) |
| Colistin\_44144393 | 44144393 | -7.575 | 1.546 | ARG261 (H\_pdon, 2.97 Ã…, 125.7Â°); SER81 (H\_pdon, 2.50 Ã…, 133.7Â°); TRP221 (H\_pdon, 3.45 Ã…, 113.2Â°); TYR112 (H\_ldon, 2.63 Ã…, 129.8Â°); TYR112 (H\_ldon, 2.98 Ã…, 127.9Â°); TYR112 (Hydrophobic, 3.27 Ã…); TYR112 (Hydrophobic, 3.75 Ã…) |
| Meropenem\_441130 | 441130 | -7.405 | 3.159 | ARG261 (Salt, 4.08 Ã…); LYS84 (H\_pdon, 2.78 Ã…, 153.0Â°); SER81 (H\_ldon, 2.15 Ã…, 122.3Â°); SER81 (H\_pdon, 2.92 Ã…, 101.1Â°); SER81 (H\_pdon, 3.31 Ã…, 128.6Â°); TRP221 (Pi); TYR112 (Hydrophobic, 3.75 Ã…) |
| Minocycline\_54675783 | 54675783 | -7.631 | 3.199 | ARG261 (H\_pdon, 2.00 Ã…, 154.8Â°); ARG261 (H\_pdon, 2.09 Ã…, 151.6Â°); TRP221 (Hydrophobic, 3.69 Ã…); TYR112 (Hydrophobic, 3.60 Ã…); TYR112 (Hydrophobic, 3.71 Ã…) |
| Ampicillin\_6249 | 6249 | -7.716 | 3.525 | ARG261 (H\_pdon, 2.17 Ã…, 150.5Â°); ARG261 (H\_pdon, 2.29 Ã…, 145.1Â°); ARG261 (Salt, 4.81 Ã…); SER81 (H\_pdon, 2.15 Ã…, 130.2Â°); TRP221 (H\_ldon, 2.07 Ã…, 139.2Â°); TRP221 (Hydrophobic, 3.68 Ã…); TYR112 (Hydrophobic, 3.60 Ã…) |

Only short list compound mention here (on the basis of docking score and interactions). This shortlisting was done on the above table of compounds. The composite score was calculated by the aforementioned code file

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ligand Name** | **CID** | **Binding Affinity** | **Interaction Score** | **Key Interactions** | **Composite Score** |
| Sophoraflavanone G\_72936 | 72936 | -8.695 | 2.51 | ARG261 (H\_pdon, 2.10 Ã…, 152.3Â°); ARG261 (H\_pdon, 2.44 Ã…, 138.0Â°); LYS84 (H\_pdon, 3.40 Ã…, 126.1Â°); SER81 (H\_pdon, 2.10 Ã…, 119.2Â°); TRP221 (Hydrophobic, 3.69 Ã…); TRP221 (Hydrophobic, 3.90 Ã…); TYR112 (Hydrophobic, 3.56 Ã…); TYR112 (Hydrophobic, 3.77 Ã…) | 0.444626 |
| Carnosol\_442009 | 442009 | -8.086 | 4.489 | ARG261 (H\_ldon, 3.12 Ã…, 127.3Â°); ARG261 (H\_pdon, 2.23 Ã…, 164.7Â°); ARG261 (H\_pdon, 3.01 Ã…, 136.3Â°); TRP221 (H\_ldon, 2.16 Ã…, 178.2Â°); TRP221 (H\_pdon, 2.11 Ã…, 128.3Â°) | 0.505518 |
| Corilagin\_73568 | 73568 | -8.816 | 2.84 | MET223 (H\_pdon, 2.20 Ã…, 166.6Â°); SER81 (H\_ldon, 2.29 Ã…, 145.4Â°); SER81 (H\_pdon, 3.12 Ã…, 109.9Â°); TRP221 (H\_ldon, 2.07 Ã…, 126.0Â°); TYR112 (H\_pdon, 3.20 Ã…, 123.9Â°) | 0.513969 |
| Rutin\_5280805 | 5280805 | -8.893 | 2.87 | ARG261 (H\_pdon, 2.37 Ã…, 155.0Â°); ARG261 (H\_pdon, 2.97 Ã…, 151.0Â°); ARG261 (Salt, 4.28 Ã…); TRP221 (H\_ldon, 2.56 Ã…, 132.4Â°); TRP221 (H\_pdon, 2.16 Ã…, 127.7Â°); TRP221 (Hydrophobic, 3.85 Ã…); TRP221 (Hydrophobic, 3.86 Ã…); TYR112 (Hydrophobic, 3.74 Ã…); TYR112 (Hydrophobic, 3.80 Ã…) | 0.537826 |
| Afzelin\_5316673 | 5316673 | -8.11 | 4.962 | ARG261 (H\_pdon, 2.73 Ã…, 161.2Â°); ARG261 (H\_pdon, 3.12 Ã…, 163.8Â°); ARG261 (Salt, 4.44 Ã…); SER81 (H\_ldon, 2.10 Ã…, 140.0Â°); TRP221 (H\_pdon, 2.11 Ã…, 127.0Â°); TYR112 (Hydrophobic, 3.80 Ã…); TYR112 (Pi) | 0.565167 |
| Myricetin\_5281672 | 5281672 | -8.234 | 5.328 | ARG261 (H\_ldon, 2.55 Ã…, 101.0Â°); ARG261 (H\_pdon, 2.00 Ã…, 151.0Â°); ARG261 (H\_pdon, 2.30 Ã…, 172.6Â°); SER81 (H\_ldon, 2.41 Ã…, 125.6Â°); TRP221 (H\_pdon, 2.34 Ã…, 130.5Â°); TYR112 (H\_ldon, 2.83 Ã…, 171.6Â°); TYR112 (H\_pdon, 3.02 Ã…, 141.5Â°); TYR112 (Hydrophobic, 3.76 Ã…) | 0.639362 |
| Procyanidin B5\_124017 | 124017 | -9.59 | 2.97 | ARG261 (H\_pdon, 2.09 Ã…, 150.3Â°); ARG261 (H\_pdon, 2.30 Ã…, 142.8Â°); SER81 (H\_pdon, 2.53 Ã…, 130.8Â°); TRP221 (Hydrophobic, 3.81 Ã…); TYR112 (H\_pdon, 3.03 Ã…, 139.8Â°); TYR112 (Hydrophobic, 3.63 Ã…) | 0.734459 |

The final screening was done via ADMET properties. Assessments were based on the following criteria:

PROPERTY\_RULES = [

    ('Muegge', 'Muegge #violations', '<=', 2),

    ('BA', 'Bioavailability Score', 'range', (0.55, 0.90)),

    ('SA', 'Synthetic Accessibility', '<=', 7),

    ('LogP', 'Consensus Log P', '<=', 4.5),

    ('Sw', 'ESOL Solubility (mg/ml)', '>=', 0.010),

    ('LogS', 'ESOL Log S', 'range', (-6.0, 0.5)),

    ('Fsp³', 'Fraction Csp3', '>', 0.36)

]

guides = {

        "MolecularWeight": 500,

        "HBondAcceptorCount": 10,

        "HBondDonorCount": 5,

        "RotatableBondCount": 10,

        "TPSA": (20, 130),

        "XLogP": (-1.0, 5.6)

    }

We see two sets of screening rules, as it was done in steps. The earliest set of 118 compounds was initially screened by the guide's dictionary, allowing no more than 3 violations to pass. This discarded the first 7 compounds (**for details on the specific compounds and their violations, visit output/primary\_lipinski\_discarded\_compounds.json**), leaving behind 111 compounds.

The final set of 7 compounds that passed both docking and plip screening were then screened by the dictionary named PROPERTY\_RULES, eliminating 3 compounds. The final set of compounds after all phases of screening is presented below.

Perform only for those compounds that you short list above

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| s.no | Ligands code | smiles | formula | mw | Rotatable h-bond | h-bond acceptor | h-bond  donar | Logp | TPSA) | Human oral absorption | Logs (predictedwater solubility |  |
| 1 |  |  |  |  |  |  |  |  |  |  |  |  |
| 2 |  |  |  |  |  |  |  |  |  |  |  |  |
| Standard antibiotics |  |  |  |  |  |  |  |  |  |  |  |  |
| Recommended values |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |

Short list compound that have similar properties as standard drugs and fall in the recommended values.

