**Table 1: Docking results of standard ligands**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Sl. No.** | **Name**  **(pubchem CID)** | **Molecular weight** | **Binding Energy**  **Kcal/mol** | **Residues interacted** |
| 1. | Penicillin  2349 | 334.4 g/mol | -7.1 | LYS A:211, ASN A: 220, ASN A:76, HIS A:250, HIS A:122, HIS A:189, SER A:217, SER A:251, ZN A:301, ZN A:301, ZN A:302, VAL A:73 |
| 2 | Benzylpenicillin  5904 | 334.4 g/mol | -8.0 | GLY A:219, ALA A:215, LYS A:211, HIS A:250, HIS A:122, HIS A:189, ZN A:301, ZN A:302, VAL A:73 |
| 3 | Mercaptopurine  667490 | 152.1 g/mol | -5.1 | ASN A:76, GLN A:60, THR A:62, TYR A:64, ASP A:212, ASP A:43, ASP A:124, SER A: 251, , ZN A:301, HIS A:250 |
| 4 | Cyclobutanone  14496 | 70.09g/mol | -2.1 | GLN A:60, ASN A:76, TYR A:64, ASP A:124, GLN A:123, ZN A:301 |
| 5 | 1,2,3 -Triazole  67516 | 69.07g/mol | -3.4 | ASN A:76, ALA A:215, THR A:62, ASP A:124, ASP A:212, VAL A:50, HIS A:250, ZN A:301, MET A:154 |
| 6 | Sulfonamide  5333 | 172.2g/mol | -5.8 | HIS A:250, HIS A:122, HIS A:189, LYS A:211, ALA A:74, GLN A:123, ARG A:52, ASN A:220, ASN A:76, GLN A:60, SER A:251, TRP A:93, ASP A: 124, ZN A:301, ZN A:302, THR A:62, ALA A:252 |
| 7 | Ampicillin  6249 | 349.4g/mol | -4.9 | TRP A:93, HIS A:250, HIS A:122, ASN A:220, ASP A:124, GLY A:219, LYS A:211, LYS A:216, VAL A:73, PHE A:70 |
| 8 | Quercitin  5280343 | 302.2g/mol | -7.1 | ZN A:301, LYS A:211, LYS A: 216, SER A:217, ASN A:220, VAL A:73, PHE A:70,ASP A:124, ALA A:215, MET A:67 |

**Table 2: Protein Profile**

|  |  |
| --- | --- |
| **Protein name** | NDM-1 D199N with Compound 16 |
| **Protein PDB id** | **6ny7** |
| **Classification** | **HYDROLASE** |
| **Host Organism** | ***Klebsiella pueumoniae*** |
| **Expression System** | ***Escherichia coli* BL21** |
| **3d image** |  |
| **Native Ligand**  **(CID** 139033900) | **[(5,7-dibromo-2-oxo-1,2-dihydroquinolin-4-yl)methyl] phosphonic acid (L8J)** |
| **Ligand Interaction (pdb standard)** |  |
| **Residues interacted with native ligand (active site)** | MET A:67, VAL A:73, HIS A:189, LYS A:211, ASN A:220 |
| **Residues interacted by native ligand**  **(docking model)** | MET A:67, VAL A:73, HIS A:189, LYS A:211, ASN A:220 |

**Table 3: Virtual Screening results of best hits**

|  |  |  |
| --- | --- | --- |
| Compound (Pubchem CID) | IUPAC Name | Binding Energy  (Kcal/mol) |
| 103646811 | (3S)-3-hydroxypyrrolidine-1-sulfonamide | -5.1 |
| **118156306** | (3Z)-N-hydroxypenta-1,3-diene-2-sulfonamide | -5.4 |
| 156787384 | 4-fluoro-1H-pyrazole-5-sulfonamide | -5.1 |
| 136574701 | 5-methyl-1H-imidazole-4-sulfonamide | -5.1 |
| 139364956 | (1R,2R)-2-hydroxycyclopentane-1-sulfonamide | -5.4 |
| 139388953 | 4-methyl-1H-pyrazole-5-sulfonamide | -5.2 |
| 64514083 | 3-methylcyclopentane-1-sulfonamide | -5.2 |
| 139389384 | 5-methyl-1H-pyrazole-3-sulfonamide | -5.1 |
| 141764153 | 2-hydroxypyrrolidine-1-sulfonamide | -5.4 |
| 156030339 | (1R,2R)-2-methylcyclopentane-1-sulfonamide | -5.3 |
| 156530860 | 2-fluorothiophene-3-sulfonamide | -5.1 |
| 45080568 | 2-oxo-1,3-oxazolidine-3-sulfonamide | -5.3 |
| **46175386** | N-hydroxyfuran-2-sulfonamide | -5.1 |
| 65050329 | 2-methylcyclopentane-1-sulfonamide | -5.2 |
| 67028586 | 2-oxo-1,3-oxazole-3-sulfonamide | -5.1 |
| 103646815 | (3R)-3-hydroxypyrrolidine-1-sulfonamide | -5.2 |
| 17976419 | Cyclohexene sulfonamide | -5.3 |
| 7370 | Benzenesulfonamide | -5.2 |
| 75536 | Cyclohexanesulfonamide | -5.2 |
| 90142128 | 3-methylfuran-2-sulfonamide | -5.2 |

**Table 4: Toxicity prediction results of best hits**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Compund**  **(Pubchem CID)** | **Hepatotoxicity** | **Carcinogenicity** | **Immunotxicity** | **Mutagenicity** | **Cytotoxicity** |
| **103646811** | **Inactive**  **0.22** | **Inactive**  **0.48** | **Inactive**  **0.01** | **Inactive**  **0.34** | **Inactive**  **0.36** |
| **75536** | **Inactive**  **0.16** | **Inactive**  **0.44** | **Inactive**  **0.01** | **Inactive**  **0.17** | **Inactive**  **0.23** |
| **7370** | **Inactive**  **0.16** | **Inactive**  **0.46** | **Inactive**  **0.01** | **Inactive**  **0.17** | **Inactive**  **0.23** |
| **139364956** | **Inactive**  **0.26** | **Inactive**  **0.39** | **Inactive**  **0.01** | **Inactive**  **0.30** | **Inactive**  **0.27** |
| **141764153** | **Inactive**  **0.27** | **Inactive**  **0.41** | **Inactive**  **0.01** | **Inactive**  **0.33** | **Inactive**  **0.34** |
| **152760603** | **Inactive**  **0.27** | **Inactive**  **0.47** | **Inactive**  **0.01** | **Inactive**  **0.31** | **Inactive**  **0.44** |
| **156030339** | **Inactive**  **0.26** | **Inactive**  **0.47** | **Inactive**  **0.01** | **Inactive**  **0.29** | **Inactive**  **0.25** |
| **156530860** | **Inactive**  **0.25** | **Inactive**  **0.37** | **Inactive**  **0.02** | **Inactive**  **0.27** | **Inactive**  **0.22** |
| **17976419** | **Inactive**  **0.25** | **Inactive**  **0.48** | **Inactive**  **0.01** | **Inactive**  **0.30** | **Inactive**  **0.29** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **45080568** | **Inactive**  **0.48** | **Inactive**  **0.44** | **Inactive**  **0.05** | **Inactive**  **0.32** | **Inactive**  **0.39** |
| **64514083** | **Inactive**  **0.26** | **Inactive**  **0.48** | **Inactive**  **0.01** | **Inactive**  **0.29** | **Inactive**  **0.25** |
| **65050329** | **Inactive**  **0.26** | **Inactive**  **0.47** | **Inactive**  **0.01** | **Inactive**  **0.29** | **Inactive**  **0.25** |
| **67028586** | **Inactive**  **0.48** | **Inactive**  **0.44** | **Inactive**  **0.05** | **Inactive**  **0.32** | **Inactive**  **0.39** |
| **103646815** | **Inactive**  **0.22** | **Inactive**  **0.48** | **Inactive**  **0.01** | **Inactive**  **0.34** | **Inactive**  **0.36** |
| **90142128** | **Inactive**  **0.24** | **Inactive**  **0.45** | **Inactive**  **0.001** | **Inactive**  **0.28** | **Inactive**  **0.23** |
| **118156306** | **Inactive**  **0.36** | **Inactive**  **0.48** | **Inactive**  **0.01** | **Inactive**  **0.50** | **Inactive**  **0.29** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **118910321** | **Inactive**  **0.22** | **Inactive**  **0.48** | **Inactive**  **0.01** | **Inactive**  **0.35** | **Inactive**  **0.25** |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **46175386** | **Inactive**  **0.42** | **Inactive**  **0.48** | **Inactive**  **0.01** | **Inactive**  **0.43** | **Inactive**  **0.34** |

**(The values in table denote the probability of the specific toxicity occurring on administration of the compound as a drug. Compounds getting the result inactive with a probability of less than 0.49 as considered as hits)**

**Table 5: ADME Prediction results of best hits**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compund**  **(Pubchem CID)** | **MDCK Permeability** | **Pgp-inhibitor** | **PPB (plasma protein . binding)** | **BBB Penetration** | **Volume Distribution** | **CYP3A4 Inhibitor** | **CYP1A2 inhibitor** | **CL (clearance)** | **T1/2 (half life)** |
| **103646811** | **0.095** | **0.001** | **38.9%** | **0.76** | **0.69** | **0.05** | **0.01** | **6.97** | **0.62** |
| **75536** | **3-05** | **0.001** | **49.0%** | **0.98** | **0.58** | **0.09** | **0.02** | **4.02** | **0.52** |
| **7370** | **0.001** | **0.001** | **46.4%** | **0.16** | **0.59** | **0.08** | **0.47** | **0.78** | **0.30** |
| **139364956** | **0.006** | **0.001** | **32.4%** | **0.96** | **0.56** | **0.06** | **0.07** | **4.57** | **0.69** |
| **141764153** | **0.002** | **0.001** | **37.2%** | **0.81** | **1.45** | **0.05** | **0.08** | **6.1** | **0.62** |
| **152760603** | **3.2-05** | **0.009** | **19.4%** | **0.90** | **1.44** | **0.05** | **0.06** | **4.62** | **0.52** |
| **156030339** | **0.015** | **0.0** | **55.0%** | **0.90** | **0.63** | **0.08** | **0.02** | **4.39** | **0.61** |
| **156530860** | **0.001** | **0.0** | **45.2%** | **0.16** | **0.60** | **0.01** | **0.12** | **1.0** | **0.36** |
| **17976419** | **3.4-05** | **0.001** | **48.9%** | **0.81** | **0.56** | **0.01** | **0.41** | **2.14** | **0.49** |
| **45080568** | **5-05** | **0.001** | **51.6%** | **0.93** | **0.5** | **0.04** | **0.01** | **6.17** | **0.85** |
| **64514083** | **0.001** | **0.002** | **32.6%** | **0.98** | **0.69** | **0.07** | **0.01** | **5.45** | **0.56** |
| **65050329** | **0.001** | **0.0** | **55.0%** | **0.90** | **0.63** | **0.08** | **0.02** | **4.39** | **0.61** |
| **67028586** | **5-05** | **0.001** | **51.6%** | **0.93** | **0.5** | **0.04** | **0.01** | **6.1** | **0.85** |
| **103646815** | **0.005** | **0.001** | **33.8%** | **0.88** | **0.86** | **0.06** | **0.01** | **5.85** | **0.55** |
| **118156306** | **0.002** | **0.0** | **55.8%** | **0.03** | **0.98** | **0.01** | **0.05** | **7.9** | **0.8** |
| **136574701** | **7-06** | **0.001** | **32.3%** | **0.39** | **1.5** | **0.01** | **0.01** | **3.18** | **0.62** |
| **156787384** | **1.6-05** | **0.002** | **32.5%** | **0.47** | **0.81** | **0.06** | **0.01** | **3.45** | **0.55** |
| **46175386** | **0.002** | **0.0** | **51.4%** | **0.04** | **0.79** | **0.07** | **0.03** | **7.47** | **0.78** |
| **90142128** | **0.001** | **0.0** | **73.9%** | **0.06** | **1.48** | **0.01** | **0.05** | **2.62** | **0.78** |

**Ranges :**

**(** MDCK Permeability : < 2 \* 10-6 cm/s; Pgp inhibitor :0 = non inhibitor and 1 = inhibitor ;

PPB : < 90% ; BBB Penetration : 0 = BBB- and 1 = BBB+ ; Volume Distribution : 0.04-20L/kg;

CYP3A4 inhibitor : 0 = non inhibitor and 1 = inhibitor ; CYP1A2 inhibitor : 0 = non substrate

and 1 = substrate ; Clearance : Low = < 5 ml/min/kg , Moderate = 5-15 ml/min/kg , High = >

20 ml/min/kg ; t ½ : 0 = short half life and 1 = long half life **)**

**Table 6: Molecular Profile and Interactions of Best hits**

|  |  |  |  |
| --- | --- | --- | --- |
| **Compound**  **(Pubchem CID)** | **Structure and Name** | **Residues Interacted** | **Interaction Types** |
| 118156306 | (3*Z*)-N-hydroxypenta-1,3-diene-2-sulfonamide | ASN A:220, HIS A:220, ASP A:124, ZN A:301, HIS A:250, ZN A:302, HIS A:122, TRP A:93 | Vander waal bonds, carbon-hydrogen bonds, conventional Hydrogen bonds, metal acceptor interactions (ZN), pi-sulfur bonds, pi-sigma bond. |
| 139364956 | (1R,2R)-2-hydroxy cyclopentane-1-sulfonamide | ASN A:220, LEU A:218, LYS A:211, GLY A:219, HIS A:189, HIS A:250, VAL A:73 | Vanderwaal bonds, conventional Hydrogen bonds, carbon-hydrogen bonds, alkyl interactions, pi-alkyl bonds, pi-sulfur bonds, metal acceptor interactions (ZN), pi-donor hydrogen |

|  |  |  |  |
| --- | --- | --- | --- |
| 141764153 | 2-hydroxypyrrolidine-1-sulfonamide | LYS A:211, LEU A:218, ASN A:220, HIS A:189, HIS A:122, HIS A:250, GLN A:123, ZN A:301, ZN A:302, TRP A:93, ASP A:124, VAL A:73, MET A:67 | Vanderwaal bonds, conventional hydrogen bonds, carbon-hydrogen bonds, metal acceptor interactions (ZN), pi-sulfur bonds, pi-alkyl bonds, alkyl bonds, pi donor hydrogen bond |
| 156030339 | (1R,2R)-2-methylcyclopentane-1-sulfonamide | LYS A:211, SER A:217, GLY A:219, HIS A:250, HIS A:189, ASN A:220, TRP A:93, VAL A: 73, MET A:67, ASP A: 124, ZN A:301, ZN A: 302, LEU A:218 | Vanderwaal bonds, conventional hydrogen bonds, alkyl bonds, pi-alkyl bonds, carbon-hydrogen bonds, pi-sulfur bonds, metal acceptor interactions (ZN) |
| 156530860 | 2-fluorothiophene-3-sulfonamide | HIS A:250, HIS A:189, HIS A:122, ASP A:124, TRP A:93, ZN A:301, ZN A:302, ASN A: 220, VAL A: 73, TRP A:93, GLN A:123 | Vanderwaal bonds, conventional hydrogen bonds, carbon-hydrogen bonds, pi-alkyl bonds, pi-sulfur bonds, pi-anion bonds, metal acceptor interactions (ZN), halogen interactions(F), pi-pi stacked bonds, pi-pi T-shaped, pi-cation bonds. |
| 45080568 | 2-oxo-1,3-oxazolidine-3-sulfonamide | GLN A:123, ASP A: 124, LYS A:211, HIS A:250, HIS A:189, HIS A:120, ASN A:220, LEU A:218, ZN A:301, ZN A:302, TRP A:93 | Vanderwaal bonds, conventional Hydrogen bonds, carbon-hydrogen bonds, pi-sulfur bonds, metal acceptor interactions (ZN). |
| 67028586 | 2-oxo-1,3-oxazole-3-sulfonamide | ZN A:301, ZN A:302, LYS A:211, HIS A:189, HIS A:122, HIS A:250, ASP A:124, ASN A:220, GLN A:123, TRP A:93, VAL A:73, MET A:67 | Vanderwaal bonds, conventional Hydrogen bonds, carbon-hydrogen bonds, pi-sulfur bonds, pi-pi T shaped, metal acceptor interactions (ZN), pi-alkyl bond, pi-anion bonds, pi-pi stacked bonds, pi-cation bond |
| 7370 | Benzenesulfonamide | TRP A:93, VAL A:73, ASP A:124, ASN A:220, HIS A:189, HIS A:122, HIS A:250, ZN A:301, ZN A:302, GLN A:123, LYS A:211, LEU A:218 | Vanderwaal bonds, conventional Hydrogen bonds, carbon-hydrogen bonds, metal acceptor interactions (ZN), pi-sulfur bonds, pi-pi T shaped bonds, alkyl bonds, pi-pi stacked, pi-cation bonds, pi-anion bond, pi donor hydrogen bond. |
| 75536 | Cyclohexanesulfonamide | TRP A:93, HIS A:189, HIS A:122, HIS A:250, ASN A: 220, ASP A:124, ZN A:301, ZN A:302, VAL A:73, LYS A:211, LEU A:218 | Vanderwaal bonds, conventional Hydrogen bonds, carbon-hydrogen bonds, pi-alkyl bonds, pi-sulfur bonds, alkyl bonds, metal acceptor interactions (ZN), pi-sigma bonds. |
| 46175386 | N-hydroxyfuran-2-sulfonamide | LYS A:211, ASN A:220, HIS A:250, HIS A:189, HIS A:122, ASP A:124, ZN A:301, ZN A:302, VAL A:73, TRP A:93, CYS A:208, LEU A:218 | Vanderwaal bonds, conventional Hydrogen bonds, pi-cation bond, pi-anion bonds, pi-pi stacked bonds, pi-alkyl bonds, carbon-hydrogen bonds, pi-sulfur bonds, metal acceptor interacions(ZN), pi-pi T-shaped |
| 65050329 | 2-methylcyclopentane-1-sulfonamide | LYS A:211, SER A:217, GLY A:219, HIS A:189, HIS A:122, HIS A:250, ASP A:124, GLN A:123, TRP A:93, ASN A:220, VAL A:73, MET A:67, ZN A:301, ZN A:302 | Vanderwaal bonds, conventional hydrogen bonds, carbon-hydrogen bonds, pi-sulfur bonds, metal acceptor interactions(ZN), pi-alkyl bonds, alkyl bonds, pi donor hydrogen bond, pi-sigma bond. |