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In Silico Exploration of Hsp90 as a Therapeutic Target in Skin Cancer: Computational Perspectives

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Abstract
Skin cancer is a serious global health concern that is on the rise and for which there are few viable treatments when the disease reaches later stages. Heat shock protein 90 (Hsp90) has emerged as a critical molecular chaperone in the stability and function of multiple client proteins, including those associated to skin cancer, that are implicated in the start and spread of cancer. This abstract provides an overview of Hsp90's involvement in the etiology of skin cancer and discusses the therapeutic potential of targeting Hsp90 as a therapeutic approach. Preclinical research using small molecule inhibitors and molecular methods has demonstrated encouraging anti-cancer effects by disrupting Hsp90-client protein interactions. Skin cancer cells die as a result of this, as well as the disruption of carcinogenic signaling pathways. Hsp90 inhibitors may also be used in combination therapy in clinical settings, as evidenced by their synergistic benefits with conventional treatments. However, because of challenges such drug resistance and off-target consequences, further study is needed to improve Hsp90-targeted therapies for skin cancer. Concentrating on Hsp90 provides a feasible route for the development of innovative therapeutic approaches to combat skin cancer and improve patient outcomes. While less common in people of color than in light-skinned Caucasians, skin cancer is frequently linked to higher rates of morbidity and death. among order to increase the chance of early tumor diagnosis, doctors must learn about skin cancer among people of color. Squamous cell carcinoma is more common in ethnic groups with darker skin; melanoma and squamous cell carcinoma typically develop on non-sun-exposed locations; and ultraviolet light is not a significant etiologic factor for skin cancer, except fors basal cell carcinoma.

Keywords: Hsp90's, Skin Cancer, Therapeutic, Chaperone.

INTRODUCTION

All eukaryotic cells include the highly conserved molecular chaperone protein known as heat shock protein 90 (Hsp90), which is essential for preserving cellular homeostasis, particularly in stressful situations like heat shock or toxin exposure. Essential biological functions like cell cycle progression, apoptosis, and signaling pathway activation are regulated by Hsp90. As a result, Hsp90 has become a desirable therapeutic target for the management of cancer. Oncoproteins degrade as a result of Hsp90's

chaperone function being disrupted by small molecule inhibitors. Its role in controlling the quality of proteins is essential, especially in times of cellular stress when it keeps its client proteins folded correctly and functional. Hsp90 is commonly overexpressed in cancer and used by tumor cells to sustain the stability and function of oncogenic proteins, which promotes tumor development, metastasis, and resistance to treatment. Hsp90 is commonly overexpressed in cancer and used by tumor cells to sustain the stability and function of oncogenic proteins, which promotes tumor development, metastasis, and resistance to treatment. Hsp90 is essential in the development of skin cancer because it stabilizes oncogenic proteins, such as kinases, transcription factors, and signaling molecules, which in turn enhances the angiogenesis, survival, and proliferation of tumor cells.Hsp90 promotes skin cells' malignant transformation and aids in tumor growth. Furthermore, through controlling angiogenic factors and proteins linked to metastasis, Hsp90 plays a role in tumor angiogenesis and metastasis. As a result, focusing on Hsp90 has become an attractive therapeutic approach for the management of skin cancer. Hsp90 is a desirable therapeutic target for the treatment of skin cancer because it regulates the stability and activity of oncogenic proteins, which is a crucial part of the disease's pathogenesis. Because Hsp90 is so important in promoting the development of skin cancer, it is a desirable target for therapeutic intervention meant to interfere with carcinogenic signaling pathways and dismantle resistance mechanisms.

Heat shock protein 90 (Hsp90) is an essential molecular chaperone involved in a variety of cellular functions in diverse animals. Hsp90 is highly conserved and expressed in a wide range of species, from bacteria to mammals, with a mass of about 90 kilodaltons. From bacteria to mammals, Hsp90 is expressed and highly conserved in a diverse spectrum of species. It is found in various isoforms, including Hsp90α and Hsp90β, each having unique roles and locations inside the cell. Hsp90 promotes protein folding, stabilizes proteins during heat stress, and facilitates the breakdown of proteins. Because it is noteworthy for stabilizing proteins necessary for tumor growth, Hsp90 inhibitors are a focus of study for anti-cancer drugs. The heat shock protein family, which includes this chaperone protein, shields cells from stressors like high temperatures. Conserved domains with distinct roles, such as the middle domain (MD), C-terminal domain (CTD), and N-terminal domain (NTD), are part of the structure of hsp90. Determining the significance of Hsp90 in cellular processes such as signal transduction, protein breakdown, and cell survival requires an understanding of its structure, regulation, and activities.

In comparison to normal cells, skin cancer cells exhibit noticeably greater levels of Hsp90 expression. This overexpression is linked to a more aggressive malignancy profile and a worse prognosis. Mutant oncoproteins, which are implicated in the unchecked growth and proliferation of cancer cells, are the cause of the elevated expression of Hsp90 in skin cancer cells. These oncoproteins are likewise client proteins of Hsp90, and skin cancer advances as a result of their association with Hsp90, which increases their stability and activity. Hsp90 has been shown to encourage tumor development and progression in skin cancer, and patient survival and prognosis are negatively correlated when its expression is present. Hsp90 inhibitors have a strong affinity for Hsp90 in tumor cells, which suggests that they may be useful as a cancer treatment approach. Hsp90 inhibitors have been demonstrated to cause autophagy and apoptosis in cancer cells, which inhibits the growth and progression of tumors in skin cancer. Hsp90 inhibitors have also been demonstrated to interfere with Hsp90's ability to operate in cancer cells while having no effect on Hsp90 in normal cells. The reason behind the selective inhibition of Hsp90 in cancer cells is the existence of multichaperone complexes, which enhance Hsp90's ATPase activity and elevate

its inhibitory affinity. To sum up, Hsp90 is an essential molecular chaperone that has a major impact on the onset and spread of skin cancer. When compared to normal cells, skin cancer cells express it at a considerably higher level. This overexpression is linked to a more aggressive malignancy profile and a worse prognosis. Hsp90 inhibitors have demonstrated promise as a cancer therapeutic approach because of their strong affinity for Hsp90 in tumor cells, which stops tumor development and metastasis. To completely comprehend the function of Hsp90 in skin cancer and to create potent Hsp90 inhibitors as a cancer treatment approach, more investigation is required. The hsp90 protein has multiple roles in the development of skin cancer. First off, Hsp90 plays a crucial role in the folding, stability, and degradation of proteins—all important processes in the initiation, development, and progression of cancer. Hsp90 is necessary for skin wound healing in skin cancer, and skin cancer cells express it far more than normal cells do. Mutant oncoproteins produced in cancer cells, which are implicated in unchecked growth and proliferation, interact with Hsp90. These oncoproteins are likewise client proteins of Hsp90, and skin cancer advances as a result of their association with Hsp90, which increases their stability and activity. 'Oncogene addiction' refers to the fact that skin cancer tumor cells become reliant on Hsp90 for life because to the considerably enhanced concentration and activity of client oncoproteins. By binding with mutant oncoproteins, enhancing their stability and activity, and raising the concentration and activity of client oncoproteins, the Hsp90 protein aids in the development of skin cancer. Extracellular Hsp90 also promotes angiogenic activity and increases skin cell motility, which in turn. supports many of the characteristics of cancer, such as tumor cell migration and invasion.

Hsp90 Structure and Domains

Three primary domains make up the highly conserved molecular chaperone protein Hsp90:

- The ATP-binding site, which is essential for Hsp90's ATPase activity and conformational alterations, is located in the N-terminal domain (NTD).
- Middle domain (MD): Affected by ATPase activity regulation and client protein binding in Hsp90. Tetratricopeptide repeat (TPR) motif found in the C-terminal domain (CTD) facilitates interactions with co-chaperones.

Hsp90 Functions

Hsp90 is essential to many different biological functions, including:

- Folding and Stabilization of Proteins: Hsp90 helps client proteins, many of which are carcinogenic—fold correctly. In the face of heat stress and other destabilizing circumstances, it stabilizes client proteins.
- Protein Degradation: Hsp90 interacts with the proteasomal machinery to facilitate the degradation of misfolded or damaged proteins.
- Signal Transduction: By stabilizing and activating important signaling proteins, Hsp90 contributes to the control of signaling pathways.
- Immune Response: Dendritic and antigen-presenting cells are activated by Hsp90, which aids in the adaptive immune response.

Hsp90 in Cancer

Oncogenic Client Proteins: Hsp90 interacts with and stabilizes numerous mutated oncoproteins, promoting their activity and contributing to cancer progression.

Tumor Selectivity: Cancer cells exhibit a higher dependence on Hsp90 for their survival and proliferation, making them more susceptible to Hsp90 inhibition.

Extracellular Hsp90 (eHsp90): A number of cancer hallmarks, including tumor cell migration, invasion, and angiogenesis, are supported by secreted Hsp90 (eHsp90).

REVIEW OF LITERATURE

1. **Sakkiah S, *et al.*, (2011)** To find a strong candidate to limit HSP90 activity, it will be useful to identify key chemical characteristics of Heat Shock Protein 90 (HSP90) inhibitors. Using Discovery Studio and Ligand Scout, respectively, the best hypothesis from Hip-Hop, Hypo1, one hydrogen bond donor (HBD), two hydrogen bond acceptors (HBA), and two hydrophobic (H) and structure-based hypothesis, SB_Hypo1, one HBA, one HBD, and four H characteristics, were produced. The best hypotheses were verified by test and decoy sets, and the chemical databases were screened using the verified hypotheses. The screened molecules were then further filtered using molecular docking, ADMET, and the rule of five. Ultimately, four new compounds that limit HSP90 activity were discovered.
2. **Kandasamy S, *et al.*, (2012)** The purpose of this study was to identify the main secondary metabolites produced by the fungus Trichoderma and evaluate them against a protein associated with skin cancer. Eighty percent methanol was used to extract the metabolites from the Trichoderma fungal biomass that was separated from the mangrove silt. After the crude methanol extract was purified, GC-MS was used to identify any secondary metabolites. Using the in-silico docking approach, three major chemicals found in the extracts—heptadecanoic acid, 16 methyl-, methyl ester; 9,12-octadecadienoic acid; and cis-9-octadecenoic acid—were tested against the skin cancer protein (Hsp90). With a docking score of − 1 1. 4 5 9 2 Kcal/mol, heptadecanoic acid, 16 methyl, methyl ester, was the most powerful of the compounds. This number was superior to "dyclonine," the recommended medication. This study suggests the 16 methyl heptadecanoic acid.
3. **Zhang Y, *et al.*, (2019)** In this work, we have synthesized and studied a series of derivatives of N-benzoyl-N′-phenyl thiourea using FTIR, elemental analysis, NMR, and X-ray single crystal diffraction. Nsingle bondH···O, Nsingle bondH···S, Csingle bondH···O, Csingle bondH···S hydrogen bonds and π···π interactions in crystal were used to demonstrate intermolecular interactions. Additionally, it was found that these compounds had antifungal action against Cercospora brassicicola P. Hennings, Fusarium graminearum, Botryosphaeria ribis, and Botryosphaeria berengriana. Hsp90 protein and target ligands were used in molecular docking to explore anti-cancer medicines 1–8. In order to assess the bioavailability of thioureas, criteria such as drug-likeness, ADME properties, toxicity effects (mutagenic, tumorigenic, irritating, and reproductive), and drug scores were computed. Comparing compound 4 to conventional medications, the results demonstrate that it has good antifungal action, and compound 5 has the potential to.
4. **Boopathy NS, *et al.*, (2010)** Over 90% of the ocean's biomass is made up of marine flora, which includes bacteria, actinobacteria, cyanobacteria, fungi, microalgae, seaweeds, mangroves, and other halophytes. Their taxonomy diversity, high productivity, biological activity, and distinct chemical makeup present a wealth of opportunities for the development of novel anticancer medications. The marine floras are abundant in compounds with therapeutic potential, primarily from the polyphenol and sulphated polysaccharide families. Numerous pharmacological characteristics, including antioxidant, immunostimulatory, and antitumor actions, have been demonstrated by the compounds. The phytochemicals may inhibit DNA oxidative damage, trigger apoptosis, and activate macrophages, all of which would limit the development of cancer. Despite having abundant chemically-enriched re-

sources, the marine flora remains poorly unexplored for lead compounds with anticancer properties. Therefore, this study examines the research that has been done on this topic to date with.

5. **Gadhi AA, *et al.*, (2018)** Because of their antifouling defense, marine macroalgae typically prevent fouling organisms from growing on their surface. Secondary metabolite formation has been linked to antifouling activity. The macroalga Halimeda sp., which was taken from the coastal waters of the Red Sea, was evaluated for its antifouling efficacy in this study utilizing extracts made by surface extraction, wet sample extraction, and dry sample extraction. The impact of solvents on bioactivity was evaluated using the solvents methanol and hexane. The macroalga extracts were found to have an inhibitory effect on the growth and settling of a bacterial strain that forms biofilms. Even though the extracts made with various techniques and solvents displayed inhibitory properties, there was a significant amount of diversity seen throughout the various tests. The spectrophotometric experiment demonstrated the potent bacterial growth inhibitory effects of hexane extracts.
6. **M. Sangeetha, *et al.*, (2014)** Predicting the anticancer medicine from cyanobacteria members was the current study's goal. Using in silico molecular docking, several cancer target protein types and the cyanobacterial medication cryptophycin-F were paired. Comparing the cyanobacterial medication cryptophycin-F with the commercial medicament cabazitaxel was made easier with the aid of molecular docking. When cryptophycin-F was combined with different cancer receptor molecules, the energy values produced ranged from -255.14 to -330.01, whereas cabazitaxel produced values between -222.18 to -385.32. Based on the aforementioned findings, it can be said that cryptophycin-F and cabazitaxel exhibited docking energies with cancer receptor molecules that were essentially comparable. As a result, cyanobacterial medication cryptophycin-F can be used as a substitute medication to treat different types of cancer without causing any negative effects.
7. **Yang Y, *et al.*, (2011)** One intriguing method for treating cancer is to inhibit the protein chaperone Hsp90α. In this work, a series of pyrazole/isoxazole scaffold inhibitors of human Hsp90α were investigated using a molecular modeling research that combined pharmacophore model, molecular docking, and three-dimensional quantitative structure-activity relationships (3D-QSAR). The key components needed for the inhibitors' biological actions can be found in the pharmacophore model. The binding mechanism between Hsp90α and its inhibitors can be understood by the molecular docking investigation. Three distinct conformational selection and alignment procedures were used in the 3D-QSAR based on CoMFA and CoMSIA models. In terms of cross-validated q 2 values of 0.782 and 0.829 and r 2 values of 0.909 and 0.968 for CoMFA and CoMSIA, respectively, the receptor-based models produced the most statistically significant findings.The findings indicate that bulky and hydrophobic groups are needed at the 4-position of the pyrazole/isoxazole ring, and that bulky and electron-repulsive substituents of 5-amides are advantageous for increasing activity. The rational creation of novel, powerful Hsp90α inhibitors will benefit from our study.
8. **Verma E, *et al.*, (2017)** Growing rates of cancer, particularly in industrialized and emerging nations, necessitate a review of possible untapped natural medicine sources. Here, in vitro, in vivo, and in silico experiments were used to assess the anticancer potential of 9-Ethyliminomethyl-12-(morpholin-4-ylmethoxy)-5,8,13,16-tetraaza -hexacene-2,3-dicarboxylic acid (EMTAHDCA), which was isolated from fresh water cyanobacterium Nostoc sp. MGL001. Eleven cancer-related proteins (Protein Data Bank IDs: 1BIX, 1NOW, 1TE6, 2RCW, 2UVL, 2VCJ, 3CRY, 3HQU, 3NMQ, 5P21, and 4B7P) that are frequently targeted of different anticancer medications were chosen as receptors for the in silico analysis, whereas EMTAHDCA was chosen as the ligand. According to the findings of

the in silico investigation, EMTAHDCA strongly binds to each of the 11 target protein receptors. Nevertheless, even at a greater dose of 1,000 ng/mL EMTAHDCA, no IC50 value was found, indicating that the EMTAHDCA did not cause cytotoxicity in the case of normal bone marrow cells. In vivo investigations additionally demonstrated that, in comparison to the DL group, the median life duration and survival days of tumor-bearing mice treated with EMTAHDCA rose dramatically with a fold change of around 1.9 and 1.81 corresponding to dosages of 5 and 10 mg/kg body weight (B.W.) of EMTAHDCA, respectively. Since there was no discernible difference between the doses of 10 mg/kg and 5 mg/kg B.W., our data indicate that 5 mg/kg B.W. is effective. All of our results from in vitro, in silico, and in vivo assessments point to the possibility of EMTAHDCA having anticancer properties.

9. **Ferlay J, *et al.*, (2013)** The GLOBOCAN 2018 database, which was created and distributed by the International Agency for Research on Cancer (IARC), currently contains estimates of the global incidence and death from 36 cancer types as well as for all cancer types combined for the year 2018. The sources and procedures utilized to compile the cancer statistics for 185 countries are reviewed in this publication. The representativeness of the source data is a prerequisite for the validity of the national estimates, and uncertainty intervals are now included for the estimated numbers of new cancer cases and deaths across all age groups and sexes, in order to account for potential causes of bias. The main findings both internationally and by globe area are succinctly described.
10. **Gaikwad A, *et al.*, (2011)** Agents that can target cancer cell markers and apoptosis inhibitor proteins are among the criteria currently used for choosing anticancer drugs. To find appropriate anticancer drugs for the cancer targets, in silico studies are frequently utilized. The current study aims to assess the interactions between cancer target proteins and several anticancer drugs identified from marine Streptomyces. Based on prior research, nine compounds from marine Streptomyces were chosen, and an in silico molecular docking method was used to assess how these compounds interacted with cancer target proteins. Through the use of the bioinformatics docking tool PatchDock, interactions between the chosen ligand and target proteins were examined.
11. **Stern RS, *et al.*, (2010)** To estimate the 2007 person prevalence of common types of nonmelanoma skin cancer (NMSC), basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), or both, in the United States using an incidence-based mathematical model; and to compare the prevalence of skin cancer with that of other common cancers.
12. **Miller DLWeinstock, *et al.*, (2010)** Since nonmelanoma skin cancer rarely results in death, measuring its morbidity is especially crucial. The latest nationwide figures indicate that the incidence is 16 years old, despite the fact that it is rising quickly. This study aimed to assess the incidence of nonmelanoma skin cancer in the United States in 1994. The 16-year-old incidence estimates were revised to account for the population's expansion, shifting age distribution, and increases in age-adjusted incidence rates reported in two population-based studies. Incidences of nonmelanoma skin cancer are expected to range from 900,000 to 1,200,000 in the US in 1994, which is comparable to the total incidence of noncutaneous cancers.

MATERIALS AND METHOD

Structure-based virtual screening, or SBVS, is a widely used method in the field of bioinformatics. It is used to identify novel ligands that function against a specific receptor protein required for the development of a disease. The protein's three-dimensional structure and the ligand's binding to it are all

that are required. Because it only requires the three-dimensional structures of the ligand and protein, it has been shown to be superior to all other methods. Using information about the protein gleaned from its structure, this approach looks for the right ligand to inhibit a protein. SBVS have proven to be beneficial in the past several years.ch for novel medications that target particular proteins.

3D-Structure retrieval of receptor protein(Hsp90 Protein)

The three proteins that are necessary for the hsp90 protein to exist (PDB ID:-2CVJ). These proteins' crystal structures were obtained by downloading them from the Protein Data Bank. There are two chains (A, B) in the Hsp90 protein, and their resolution is 2.00 Å. Following their extraction from the protein data repository, the proteins underwent a number of processes.

Biovia Discovery Studio 2021

Dassault Systems created the potent software suite Biovia Discovery Studio especially for drug discovery and life science research. With the help of its extensive toolkit and capabilities, scientists may accurately and efficiently model, simulate, display, and evaluate biological systems (Dassault Systems, n.d.). Through the integration of multiple fields, including structural biology, cheminformatics, bioinformatics, and molecular modeling, development Studio offers researchers a comprehensive platform to expedite the drug development process. protein's three-dimensional structural visualization, created using Biovia Discovery Studio

Swiss PDB Viewer

Swiss PDB Viewer (SPDBV) is a widely used software tool developed by the Swiss Institute of Bioinformatics for visualizing and analyzing protein structures. It provides an intuitive user interface that allows researchers to explore and manipulate 3D protein structures, perform structural alignments, calculate electrostatic potentials, and generate high-quality images (Guex & Peitsch, 1997). Removal of water molecules and heteroatoms and energy minimization done on Swiss PDB Viewer

Cast-P (Active site analysis)

For additional Hsp90 protein docking, just one chain (Chain-A) was chosen, and that chain was chosen for docking. Using the Cast-P active site predictor, active sites in protein chains were identified following the selection of the protein chains. The Hsp90 protein's chain-A's active site was located at coordinates X: 4, Y: 32, Z: 11. The grid box's dimensions were X: 40, Y: 40, Z: 40, with a 0.408 Å spacing between each value. Following the discovery of active sites on the protein chains, the PDBQT format was used to store the protein structures for docking.

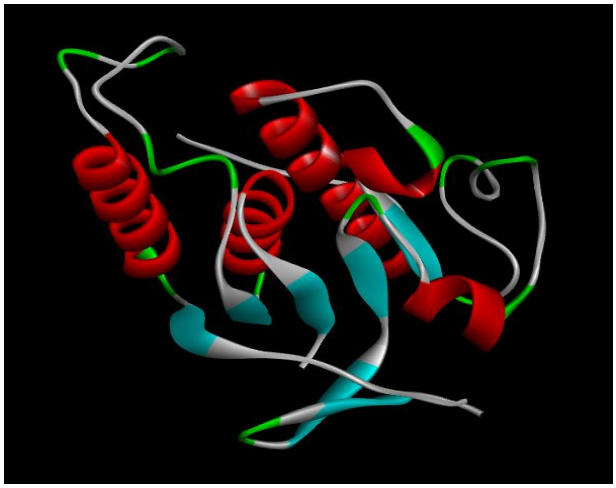

Fig.01: 3D Structure of receptor protein's (Hsp90 protein)

Ligand preparation:

Random ligand selection was used to find ligands that inhibited the Hsp90 protein in the PubChem database (https://pubchem.ncbi.nlm.nih.gov). We used five similar approaches (Pharmacophore) based on similarities, and 200 ligands were found. In order to confirm the ligands' drug-like qualities, ADME and RO5 screens were performed on them after they were extracted from the database.

S.No	CHEMBL ID	FORMULA	CANONICAL SMILES ID
1	CHEMBL1939719	C44H67N17O9	CN(CCCC(=O)NCCCCn1nnc2c1CCCCCC2OCCNC(=O)CCCN(C)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O
2	CHEMBL4095543	C28H38N8O3	C[C@H](NC1CC(CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1)[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O
3	CHEMBL524037	C25H35N7O7	O=CNc1cc(C(O)CNCCCCCCNc2ncnc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)ccc1O
4	CHEMBL4082140	C32H44N8O3	C[C@@H]([C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)N(C1CCC1)C1CC(CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1
5	CHEMBL4100144	C45H60N10O3	C[C@@H]([C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)N(C1CC(CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1)C1CC(CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1
6	CHEMBL4096796	C27H33N7O5S	Nc1ccc(c2cccc(C(=ONCCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)c2)s1
7	CHEMBL3087499	C30H42N8O3	CC(C)N(C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C1CC(CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1
8	CHEMBL4079133	C30H42N8O3	CC(C)N(C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)[C@H]1C[C@H](CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1
9	CHEMBL3414626	C30H42N8O3	CC(C)N(C[0C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)[C@H]1C[C@@H](CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1

10	CHEMBL4081224	C34H36F3N7O5S	Nc1cc(c2cccc(C(F(FFc2c(c2ccc(C(=ONCCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc2)s1
11	CHEMBL370571	C34H45N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1CC(CCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
12	CHEMBL4076495	C34H37N7O6S	Nc1sc(c2ccc(C(=ONCCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc2)cc1C(=O)c1ccccc1
13	CHEMBL4072009	C41H40F3N7O6S	Nc1sc(c2ccccc2C(=ONCCCCCCNc2ncnc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)c(c2cccc(C(F)(F)F)c2)c1C(=O)c1ccccc1
14	CHEMBL369588	C35H47N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1C[C@H](CCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
15	CHEMBL371948	C37H51N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1C[C@H](CCCCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
16	CHEMBL261527	C37H51N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1CC(CCCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
17	CHEMBL332756	C36H49N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1C[C@H](CCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
18	CHEMBL4104819	C41H40F3N7O6S	Nc1sc(c2ccc(C(=ONCCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc2)c(c2cccc(C(F)(F)F)c2)c1C(=O)c1ccccc1
19	CHEMBL372560	C38H53N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1C[C@H](CCCCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@

			@H]2O
20	CHEMBL170583	C39H55N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1C[C@H](CCCCCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
21	CHEMBL331544	C39H55N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1C[C@@H](CCCCCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
22	CHEMBL382114	C39H55N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1CC(CCCCCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
23	CHEMBL198558	C40H57N5O7	C[C@]12CC[C@@H]3c4ccc(O)cc4CC[C@H]3[C@@H]1C[C@H](CCCCCCCCCCCC(=O)OC[C@H]1O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]1O)[C@@H]2O
24	CHEMBL4063841	C40H38F3N7O6S	Nc1sc(c2ccc(C(=ONCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc2)c(c2cccc(C(F)(F)F)c2)c1C(=O)c1ccccc1
25	CHEMBL4101850	C41H40F3N7O6S	Nc1sc(c2cccc(C(=ONCCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)c2)c(c2cccc(C(F)(F)F)c2)c1C(=O)c1ccccc1
26	CHEMBL4077152	C41H39ClF3N7O6S	Nc1sc(c2ccc(C(=ONCCCCCCNc3nc(Cl)nc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc2)c(c2cccc(C(F)(F)F)c2)c1C(=O)c1ccccc1
27	CHEMBL4075186	C42H42F3N7O6S	Nc1sc(c2ccc(C(=ONCCCCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc2)c(c2cccc(C(F)(F)F)c2)c1C(=O)c1ccccc1
28	CHEMBL462274	C22H31N7O6	Nc1cc(C(O)CNCCCCNc2ncnc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)ccc1O

29	CHEMBL611273	C24H30N10O7	CCNC(=O)[C@H]1OC(n2cnc3c(NCCCCCCNc4ccc([N+](=O)[O])c5nonc45)ncnc32)[C@H](O)[C@@H]1O
30	CHEMBL2413113	C24H30N10O7	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(NCCCCCCNc4ccc([N+](=O)[O])c5nonc45)ncnc32)[C@H](O)[C@@H]1O
31	CHEMBL4299211	C26H43N13O6S2	CCN(CC)CC.[N]=[N+]=N[C@@H]1[C@H](O)[C@@H](CNS(=O)(=ONC(=OCCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)O[C@H]1n1cnc2c(N)ncnc21
32	CHEMBL4299213	C26H43N13O6S2	CCN(CC)CC.[N]=[N+]=N[C@H]1[C@H](O)[C@@H](CNS(=O)(=ONC(=OCCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)O[C@H]1n1cnc2c(N)ncnc21
33	CHEMBL4086624	C27H32N6O5S	O=C(NCCCCCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)c1cccc(-c2cccs2)c1
34	CHEMBL4299214	C26H43FN10O6S2	CCN(CC)CC.Nc1ncnc2c1ncn2[C@@H]1O[C@H](CNS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)[C@@H](O)[C@H]1F
35	CHEMBL1939718	C42H63N17O9	CN(CCCC(=O)NCCOC1CCCCCc2c1nnn2CCNC(=O)CCCN(C)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O
36	CHEMBL462273	C23H31N7O7	O=CNc1cc(C(O)CNCCCCNc2ncnc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)ccc1O
37	CHEMBL4089092	C34H35F3N6O5S	O=C(NCCCCCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)c1ccc(c2sccc2c2cccc(C(F)(F)F)c2)cc1
38	CHEMBL611562	C28H38N10O7	CCNC(=O)[C@H]1OC(n2cnc3c(NCCCCCCCCCCNc4ccc([N+](=O)[O])c5nonc45)ncnc32)[C@H](O)[C@@H]1O
39	CHEMBL2413115	C28H38N10O7	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(NCCCCCCCCCCNc4ccc([N+](=O)[O])c5nonc45)ncnc32)[C@H](O)[C@@H]1O
40	CHEMBL4078771	C34H36N6O6S	O=C(NCCCCCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)c1cccc(c2cc(C(=O)c3ccccc3)cs2)c1
41	CHEMBL2413114	C26H34N10O7	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(NCCCCCCCCCNc4ccc([N+](=O)[O])c5n

			onc45)ncnc32)[C@H](O)[C@@H]1O
42	CHEMBL611561	C26H34N10O7	CCNC(=O)[C@H]1OC(n2cnc3c(NCCCCCCCCNc4ccc([N+](=O)[O])c5nonc45)ncnc32)[C@H](O)[C@@H]1O
43	CHEMBL518959	C22H25N6NaO8S	O=C([N]S(=O)(=O)OC[C@H]1O[C@@H](n2cnc3c(NC4CCCC4)ncnc32)[C@H](O)[C@@H]1O)c1ccccc1O[Na+]
44	CHEMBL4299212	C26H45N11O6S2	CCN(CC)CC.Nc1ncnc2c1ncn2[C@@H]1O[C@H](CNS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)[C@@H](O)[C@H]1N
45	CHEMBL4105473	C41H39F3N6O6S	O=C(NCCCCCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)c1ccc(c2scc(C(=O)c3ccccc3)c2-c2cccc(C(F)(F)F)c2)cc1
46	CHEMBL3140272	C20H29N9O7S2	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CNS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)[C@@H](O)[C@H]1O
47	CHEMBL4442160	C31H37N7O5	OC[C@H]1O[C@@H](n2cnc3c(N4CCN(c5ccc(c6cccc(CN7CCOCC7)c6)cc5)CC4)ncnc32)[C@H](O)[C@@H]1O
48	CHEMBL3701287	C25H34N10O4S	CC1(C)O[C@@H]2[C@H](O1)[C@@H](n1cnc3c(N)ncnc31)O[C@H]2Cn1cc(CCCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)nn1
49	CHEMBL4076565	C43H42F3N7O7S	CC(=O)Nc1sc(c2ccc(C(=O)NCCCCCCNc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc2)c(c2cccc(C(F)(F)F)c2)c1C(=O)c1ccccc1
50	CHEMBL392720	C24H27ClN6O6	O=C(OCc1ccccc1Cl)N1[C@H]2CC[C@H]1[C@H](Nc1ncnc3c1ncn3[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C2
51	CHEMBL430374	C24H27BrN6O6	O=C(OCc1ccccc1Br)N1[C@H]2CC[C@H]1[C@H](Nc1ncnc3c1ncn3[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C2
52	CHEMBL4085418	C43H43F3N8O6S	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(NCCCCCCNC(=O)c4ccc(c5sc(N)c(C(=O)c6ccccc6)c5c5cccc(C(F)(F)F)c5)cc4)ncnc32)[C@H](O)[C@@H]1O
53	CHEMBL3679378	C22H26FN5O5	OC[C@H]1OC(n2cnc3c(NC4CCC[C@@H]4OCc4ccc(F)cc4)ncnc32)[C@H](O)

			[C@@H]1O
54	CHEMBL3679385	C22H26FN5O5	OC[C@H]1O[C@@H](n2cnc3c(NC4CCC[C@H]4OCc4ccc(F)cc4)ncnc32)[C@H](O)[C@@H]1O
55	CHEMBL3397329	C22H31N9O4S	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CSCC[C@H](N)C(=O)NCc2cc(C3CCC3)[nH]n2)[C@@H](O)[C@H]1O
56	CHEMBL4475410	C39H66N16O9	N=C(N)NCCC[C@H](NC(=O)[C@H](CCCCN)NC(=O)[C@@H]1CCCN1C(=O)[C@@H]1CCCN1CCCN(CC[C@H](N)C(=O)O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C(N)=O
57	CHEMBL4069296	C41H41F3N8O6S	Nc1nc(NCCCCCCNC(=O)c2ccc(c3sc(N)c(C(=O)c4ccccc4)c3c3cccc(C(F)(F)F)c3)cc2)c2ncn([C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)c2n1
58	CHEMBL562056	C20H22Br2N10O6S2	Nc1ncnc2c1nc(Br)n2[C@@H]1O[C@H](CSSC[C@H]2O[C@@H](n3c(Br)nc4c(N)ncnc43)[C@H](O)[C@@H]2O)[C@@H](O)[C@H]1O
59	CHEMBL560315	C20H23BrN10O6S2	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CSSC[C@H]2O[C@@H](n3c(Br)nc4c(N)ncnc43)[C@H](O)[C@@H]2O)[C@@H](O)[C@H]1O
60	CHEMBL1098507	C19H32N6O4	CC1(C)CC(NC2NC=Nc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)CC(C)(C)N1
61	CHEMBL4299217	C26H42FN9O7S2	CCN(CC)CC.Nc1ncnc2c1ncn2[C@@H]1O[C@H](COS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)[C@@H](O)[C@@H]1F
62	CHEMBL1090688	C40H47Cl2N7O6S	Nc1sc2c(c1C(=O)c1ccc(Cl)c(Cl)c1)CCN(CCCCCCCCCCOc1ccc(Nc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc1)C2
63	CHEMBL4299210	C27H46N10O6S2	CCN(CC)CC.Nc1ncnc2c1ncn2[C@@H]1C[C@H](CNS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)[C@@H](O)[C@H]1O

64	CHEMBL1939725	C44H69I2N17O9	C[N+](C)(CCCC(=O)NCCOC1CCCCCc2c1nnn2CCNC(=O)CCC[N+](C)(C)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O.[I-].[I-]
65	CHEMBL1939723	C36H56N14O8	CN(CCCC(=O)NCCCCCCNC(=O)CCCN(C)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O
66	CHEMBL3679388	C23H29N5O6	COc1cccc(CO[C@@H]2CCCC2Nc2ncnc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)c1
67	CHEMBL3679377	C22H26FN5O5	OC[C@H]1OC(n2cnc3c(NC4CCC[C@@H]4OCc4cccc(F)c4)ncnc32)[C@H](O)[C@@H]1O
68	CHEMBL3679381	C23H29N5O6	COc1cccc(CO[C@H]2CCCC2Nc2ncnc3c2ncn3C2O[C@H](CO)[C@@H](O)[C@H]2O)c1
69	CHEMBL3679384	C22H26FN5O5	OC[C@H]1O[C@@H](n2cnc3c(NC4CCC[C@H]4OCc4cccc(F)c4)ncnc32)[C@H](O)[C@@H]1O
70	CHEMBL240487	C24H28N6O6	O=C(OCc1ccccc1)N1[C@H]2CC[C@H]1[C@H](Nc1ncnc3c1ncn3[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C2
71	CHEMBL1090687	C39H45Cl2N7O6S	Nc1sc2c(c1C(=O)c1ccc(Cl)c(Cl)c1)CCN(CCCCCCCCCOc1ccc(Nc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc1)C2
72	CHEMBL1090686	C38H43Cl2N7O6S	Nc1sc2c(c1C(=O)c1ccc(Cl)c(Cl)c1)CCN(CCCCCCCCOc1ccc(Nc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc1)C2
73	CHEMBL589264	C39H49ClN12O4S	CNC(=O)[C@@]12C[C@@H]1[C@@H](n1cnc3c(NCc4cccc(Cl)c4)nc(C#CCCCCc4cn(CCCCCCNC5SCC6NC(=O)NC65)nn4)nc31)[C@H](O)[C@@H]2O
74	CHEMBL611766	C31H44N10O8S	CCN(CC)CC.Nc1nc(n2cc(C3CCCCC3)nn2)nc2c1ncn2[C@@H]1O[C@H](COS(=O)(=O)NC(=O)c2ccccc2O)[C@@H](O)[C@H]1O

75	CHEMBL4539148	C24H26F2N8O4	OC[C@H]1O[C@@H](n2cnc3c(N4CCN(c5ccc(c6cnn(C(F)F)c6)cc5)CC4)ncnc32)[C@H](O)[C@@H]1O
76	CHEMBL4463459	C26H26F3N7O4	OC[C@H]1O[C@@H](n2cnc3c(N4CCN(c5ccc(c6ccc(C(F)(F)F)nc6)cc5)CC4)ncnc32)[C@H](O)[C@@H]1O
77	CHEMBL1090685	C37H41Cl2N7O6S	Nc1sc2c(c1C(=O)c1ccc(Cl)c(Cl)c1)CCN(CCCCCCCOc1ccc(Nc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc1)C2
78	CHEMBL4475059	C26H29N7O5	COc1ccc(c2ccc(N3CCN(c4ncnc5c4ncn5[C@@H]4O[C@H](CO)[C@@H](O)[C@H]4O)CC3)cc2)cn1
79	CHEMBL53795	C27H34N6O4S	C[C@H]1O[C@@H](n2cnc3c(NC4CCCC4)ncnc32)[C@H](O)[C@H]1NC(=O)C1CCCC[C@H]1C(=O)c1cccs1
80	CHEMBL4209152	C30H40N8O6S	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(NCCCCCCNS(=O)(=O)c4cccc5c(N(C)C)cccc45)ncnc32)[C@H](O)[C@@H]1O
81	CHEMBL612203	C30H40N8O6S	CCNC(=O)[C@H]1OC(n2cnc3c(NCCCCCCNS(=O)(=O)c4cccc5c(N(C)C)cccc45)ncnc32)[C@H](O)[C@@H]1O
82	CHEMBL4636288	C36H62N16O9	N=C(N)NCCC[C@H](NC(=O)[C@H](CCCCN)NC(=O)[C@@H]1CCCN1C(=O)CNCCCN(CC[C@H](N)C(=O)O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C(N)=O
83	CHEMBL459679	C21H23N6NaO8S	O=C([N]S(=O)(=O)OC[C@H]1O[C@@H](n2cnc3c(NC4CCC4)ncnc32)[C@H](O)[C@@H]1O)c1ccccc1O.[Na+]
84	CHEMBL1094353	C19H31N6O5	CC1(C)CC(NC2NC=Nc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)CC(C)(C)N1[O]
85	CHEMBL611272	C32H44N8O6S	CCNC(=O)[C@H]1OC(n2cnc3c(NCCCCCCCCNS(=O)(=O)c4cccc5c(N(C)C)cccc45)ncnc32)[C@H](O)[C@@H]1O
86	CHEMBL1090684	C36H39Cl2N7O6S	Nc1sc2c(c1C(=O)c1ccc(Cl)c(Cl)c1)CCN(CCCCCCOc1ccc(Nc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc1)C2
87	CHEMBL610121	C34H48N8O6S	CCNC(=O)[C@H]1OC(n2cnc3c(NCCCCCCCCCNS(=O)(=O)c4cccc5c(N(C)C)cccc45)ncnc32)[C@H](O)[C@@H]1O

88	CHEMBL2413110	C35H50N8O6S	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(NCCCCCCCCCCCNS(=O)(=O)c4cccc5c(N(C)C)cccc45)ncnc32)[C@H](O)[C@@H]1O
89	CHEMBL4077188	C27H34F3N7O9S2	CCCCNC(=O)c1cn([C@H]2[C@@H](O)[C@@H](CO)O[C@@H](SS[C@@H]3O[C@H](CO)[C@H](O)[C@H](n4cc(c5cc(F)c(F)c(F)c5)nn4)[C@H]3O)[C@@H]2O)nn1
90	CHEMBL240279	C21H30N6O6	CC(C)(C)OC(=O)N1[C@H]2CC[C@H]1[C@H](Nc1ncnc3c1ncn3[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C2
91	CHEMBL609105	C30H42N10O8S	CCN(CC)CC.Nc1nc(n2cc(C3CCCC3)nn2)nc2c1ncn2[C@@H]1O[C@H](COS(=O)(=O)NC(=O)c2ccccc2O)[C@@H](O)[C@H]1O
92	CHEMBL608044	C36H52N8O6S	CCNC(=O)[C@H]1OC(n2cnc3c(NCCCCCCCCCCCNS(=O)(=O)c4cccc5c(N(C)C)cccc45)ncnc32)[C@H](O)[C@@H]1O
93	CHEMBL1939722	C34H52N14O8	CN(CCCC(=O)NCCCCNC(=O)CCCN(C)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O
94	CHEMBL569224	C46H46N8O12S	O=C(CCCCCNC(=O)c1ccc2c(c1)C(=O)OC21C2=C(C=C(O)CC2)Oc2cc(O)ccc21)NCCSC[C@H]1O[C@@H](n2cnc3c(NCc4ccc([N+](=O)[O-])cc4)ncnc32)[C@H](O)[C@@H]1O
95	CHEMBL294675	C23H26N6O6	O=C(N[C@@H]1[C@@H](O)[C@H](n2cnc3c(NC4CCCC4)ncnc32)O[C@@H]1CO)c1ccc2c(c1)OCO2
96	CHEMBL4635903	C37H64N16O9	N=C(N)NCCC[C@H](NC(=O)[C@H](CCCCN)NC(=O)[C@@H]1CCCN1C(=O)CNCCCCN(CC[C@H](N)C(=O)O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C(N)=O
97	CHEMBL391031	C16H22N6O4	OC[C@H]1O[C@@H](n2cnc3c(NC4CC5CCC4N5)ncnc32)[C@H](O)[C@@H]1O
98	CHEMBL36098	C23H34N6O5	O=C(CCC1CCCC1)Nc1nc(NC2CCCC2)c2ncn([C@@H]3O[C@H](CO)[C@@H]

			(O)[C@H]3O)c2n1
99	CHEMBL1090683	C35H37Cl2N7O6S	Nc1sc2c(c1C(=O)c1ccc(Cl)c(Cl)c1)CCN(CCCCCOc1ccc(Nc3ncnc4c3ncn4[C@@H]3O[C@H](CO)[C@@H](O)[C@H]3O)cc1)C2
100	CHEMBL4566815	C29H34N6O5	CC(C)(O)c1ccc(c2ccc(N3CCN(c4ncnc5c4ncn5[C@@H]4O[C@H](CO)[C@@H](O)[C@H]4O)CC3)cc2)cc1
101	CHEMBL55099	C23H27FN6O4	Cc1ccc(C(=O)N[C@@H]2[C@@H](O)[C@H](n3cnc4c(NC5CCCC5)ncnc43)O[C@@H]2CO)cc1F
102	CHEMBL4095344	C22H29N7O3	Cc1cc(C)n(C[C@H]2O[C@@H](n3cnc4c(NC5CC6CCC5C6)ncnc43)[C@H](O)[C@@H]2O)n1
103	CHEMBL612057	C31H42N10O8S	CCN(CC)CC.Nc1nc(n2cc(C3=CCCCC3)nn2)nc2c1ncn2[C@@H]1O[C@H](COS(=O)(=O)NC(=O)c2ccccc2O)[C@@H](O)[C@H]1O
104	CHEMBL1939721	C33H50N14O8	CN(CCCC(=O)NCCCNC(=O)CCCN(C)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O
105	CHEMBL612044	C37H58N10O8S	CCCCCCCCCCCCc1cn(c2nc(N)c3ncn([C@@H]4O[C@H](COS(=O)(=O)NC(=O)c5ccccc5O)[C@@H](O)[C@H]4O)c3n2)nn1.CCN(CC)CC
106	CHEMBL3679379	C25H33N5O5	CC(C)c1ccc(CO[C@H]2CCCC2Nc2ncnc3c2ncn3C2O[C@H](CO)[C@@H](O)[C@H]2O)cc1
107	CHEMBL3769408	C19H28N6O4	CN1[C@@H]2CCC[C@H]1C[C@@H](Nc1ncnc3c1ncn3[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C2
108	CHEMBL4209821	C20H30N6O4	OC[C@H]1O[C@@H](n2cnc3c(N4CCN(C5CCCCC5)CC4)ncnc32)[C@H](O)[C@@H]1O
109	CHEMBL608748	C20H29N5O5	OC[C@H]1OC(n2cnc3c(NC4CCC5CCCCC5C4)nc(O)nc32)[C@H](O)[C@@H]1O
110	CHEMBL3679385	C22H26FN5O5	OC[C@H]1O[C@@H](n2cnc3c(NC4CCC[C@H]4OCc4ccc(F)cc4)ncnc32)[C@H](O)[C@@H]1O

111	CHEMBL3679377	C22H26FN5O5	OC[C@H]1OC(n2cnc3c(NC4CCC[C@@H]4OCc4cccc(F)c4)ncnc32)[C@H](O)[C@@H]1O
112	CHEMBL338399	C25H38N6O4	O=C(CCCC1CCCCC1)N[C@H]1C(CO)OC(n2cnc3c(NC4CCCC4)ncnc32)C1O
113	CHEMBL1823453	C22H31N5O5	O=C(OC[C@H]1O[C@@H](n2cnc3c(NC4CCCC4)ncnc32)[C@H](O)[C@@H]1O)C1CCCCC1
114	CHEMBL612210	C18H23N5O5	OC[C@H]1OC(n2cnc3c(NCC4CC5CC4C4OC54)ncnc32)[C@H](O)[C@@H]1O
115	CHEMBL2112632	C26H34N6O4	O=C(CCCCc1ccccc1)N[C@@H]1[C@@H](O)[C@H](n2cnc3c(NC4CCCC4)ncnc32)O[C@@H]1CO
116	CHEMBL2147151	C20H29N5O5	Nc1nc(OC2CCC3CCCCC3C2)nc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O
117	CHEMBL610983	C16H21N5O5	OC[C@H]1OC(n2cnc3c(NC4CCC5OC5C4)ncnc32)[C@H](O)[C@@H]1O
118	CHEMBL2364571	C17H21N5O5	OC[C@H]1O[C@@H](n2cnc3c(N[C@@H]4CC5CC4C4OC54)ncnc32)[C@H](O)[C@@H]1O
119	CHEMBL2112106	C17H21N5O5	OC[C@H]1O[C@H](n2cnc3c(NC4CC5CC4[C@H]4O[C@@H]54)ncnc32)[C@@H](O)[C@H]1O
120	CHEMBL2112185	C17H21N5O5	OC[C@@H]1O[C@H](n2cnc3c(NC4CC5CC4[C@@H]4O[C@H]54)ncnc32)[C@@H](O)[C@H]1O
121	CHEMBL2364570	C17H21N5O5	OC[C@H]1O[C@@H](n2cnc3c(N[C@H]4CC5CC4C4OC54)ncnc32)[C@H](O)[C@@H]1O
122	CHEMBL2071119	C24H33N7O3S	Cc1nc(NCC2CCN(C)CC2)nc(N[C@@H]2C[C@H](CO)[C@@H](O)[C@H]2O)c1-c1nc2cnccc2s1
123	CHEMBL1628097	C30H36N6O8	C[C@]12CC[C@@H]3c4ccc(OCCOC[C@H]5OC(n6cnc7c(N)ncnc76)[C@H](O)[C@@H]5O)c([N+](=O)[O-])c4CC[C@H]3[C@@H]1CCC2=O
124	CHEMBL4635424	C25H40N8O5	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CN(CC[C@H](N)C(=O)O)C2CN(CCCC3CCCC3)C2)[C@@H](O)[C@H]1O

125	CHEMBL2430544	C53H79N19O13	CN1CCN(c2ccc3nc(c4ccc(OCc5cn(Cn6cc(CCCCc7cn(C[C@H]8O[C@@H](O[C@@H]9[C@@H](O)[C@H](N)C[C@H](N)[C@H]9O[C@H]9O[C@H](CN)[C@@H](O)[C@H](O)[C@H]9N)[C@H](O)[C@@H]8O[C@H]8O[C@@H](CN)[C@@H](O)[C@H](O)[C@H]8N)nn7)nn6)nn5)cc4)[nH]c3c2)CC1
127	CHEMBL3674590	C23H29N5O5	Cc1ccc(CO[C@H]2CCCC2Nc2ncnc3c2ncn3C2O[C@H](CO)[C@@H](O)[C@H]2O)cc1
128	CHEMBL505023	C30H56N10O12	NC[C@@H]1O[C@H](O[C@H]2[C@@H](O)[C@H](O[C@@H]3[C@@H](O)[C@H](N)C[C@H](N)[C@H]3O[C@H]3O[C@H](CN)[C@@H](O)[C@H](O)[C@H]3N)O[C@@H]2Cn2cc(C3CCCCN3)nn2)[C@H](N)[C@@H](O)[C@@H]1O
129	CHEMBL1084430	C20H26N7O10PS	CO[C@@H]1[C@H](OP(=O)(S)OC[C@H]2O[C@@H](n3cnc4c(N)ncnc43)C[C@@H]2O)[C@@H](CO)O[C@H]1n1ccc(=O)[nH]c1=O
130	CHEMBL2002195	C36H60N5O11P	CCCCCCCCCCCCCCCCNc1ccn(C2CC(OP(=O)(O)OCC3OC(n4cc(CC)c(=O)[nH]c4=O)CC3O)C(CO)O2)c(=O)n1
131	CHEMBL2358055	C32H37N7O5	O=C(CC[C@H]1O[C@@H](n2cnc3c(NC(=O)c4ccccc4)ncnc32)[C@H](O)[C@@H]1O)NCC1CCN(Cc2ccccc2)CC1
132	CHEMBL3623647	C23H27N13O7	Nc1ncnc2c1ncn2[C@@H]1O[C@H](COCc2cn(C[C@H]3O[C@@H](n4cnc5c(N)ncnc54)[C@H](O)[C@@H]3O)nn2)[C@@H](O)[C@H]1O
133	CHEMBL1198942	C25H38N11O9P	N=C(N)NCCCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
134	CHEMBL1077566	C25H39ClN11O9P	Cl.N=C(N)NCCCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
135	CHEMBL1162403	C28H49N11O9	NC[C@H]1O[C@H](O[C@H]2[C@@H](NCCCCCCNC(=O)[C@H]3O[C@@H](n4cnc5c(N)ncnc54)[C@H](O)[C@@H

			]3O)[C@@H](O)[C@H](N)C[C@@H]2N)[C@H](N)[C@@H](O)[C@@H]1O
136	CHEMBL559921	C19H23N7O7S3	NC(=O)c1csc([C@@H]2O[C@H](CSSC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)[C@H](O)[C@@H]3O)[C@@H](O)[C@H]2O)n1
137	CHEMBL1092021	C24H37ClN11O9P	Cl.N=C(N)NCCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
138	CHEMBL1199027	C24H36N11O9P	N=C(N)NCCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
139	CHEMBL356610	C20H28N6O5S	O[C@@H]1[C@@H](CO/C(S)=N/C2CCCC2)OC(n2cnc3c(NC4CCOC4)ncnc32)[C@@H]1O
140	CHEMBL345494	C21H30N6O6	O=C(NC1CCCCC1)OC[C@H]1OC(n2cnc3c(NC4CCOC4)ncnc32)[C@H](O)[C@@H]1O
141	CHEMBL3601452	C39H51N7O10	COc1ccc(C[C@H](NC(=O)OC2CCCC3(C2)OOC2(O3)C3CC4CC(C3)CC2C4)C(=O)N[C@H]2[C@@H](O)[C@H](n3cnc4c(N(C)C)ncnc43)O[C@@H]2CO)cc1
142	CHEMBL4638041	C41H70N16O9S	CC[C@H](C)[C@H](NC(=O)[C@H](CCCNC(=N)N)NC(=O)[C@H](CCCCN)NC(=O)[C@@H]1CCCN1C(=O)CNCCCSC[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)C(=O)N[C@@H](C)C(N)=O
143	CHEMBL1928284	C24H32N12O4S	Nc1nc2ncc(CNCCN3CCC(SC[C@H]4O[C@@H](n5cnc6c(N)ncnc65)[C@H](O)[C@@H]4O)CC3)nc2c(=O)[nH]1
144	CHEMBL561654	C20H24N10O6S2	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CSSC[C@H]2O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]2O)[C@@H](O)[C@H]1O
145	CHEMBL611107	C20H24N10O6S2	Nc1ncnc2c1ncn2C1O[C@@H](CSSC[C@H]2OC(n3cnc4c(N)ncnc43)[C@H](O)[C@@H]2O)[C@H](O)[C@@H]1O
146	CHEMBL3144371	C20H25N10O8P	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CO)C[C@H]1OP(=O)(O)OC[C@H]1O[C@

			@H](n2cnc3c(N)ncnc32)C[C@@H]1O
147	CHEMBL413173	C61H107N27O14S	COCCOCCNC(=O)C(CCCCNC(=O)CCCC[C@@H]1SC[C@@H]2NC(=O)N[C@@H]21)NC(=O)[C@H](CCCN=C(N)N)NC(=O)[C@H](CCCN=C(N)N)NC(=O)[C@H](CCCN=C(N)N)NC(=O)[C@H](CCCN=C(N)N)NC(=O)CCCCCNC(=O)[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O
148	CHEMBL3770434	C20H29N7O4	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(N4[C@@H]5CCC[C@H]4C[C@H](N)C5)ncnc32)[C@H](O)[C@@H]1O
149	CHEMBL1092352	C23H35N10O8P	NCCCCNP(=O)(OC[C@H]1O[C@@H](n2cnc3c(N)ncnc32)C[C@@H]1O)O[C@H]1C[C@H](n2ccc(N)nc2=O)O[C@@H]1CO
150	CHEMBL3416848	C54H83FN6O14	CC[C@@H](C(=O)[C@@H](C)[C@@H](O)[C@H](C)[C@@H]1O[C@@H]([C@@H](CC)C(=O)NCc2cn([C@H]3C[C@H](n4cc(F)c(=O)[nH]c4=O)O[C@@H]3CO)nn2)CC[C@@H]1C)[C@H]1O[C@]2(C=C[C@@H](O)[C@]3(CC[C@@](C)([C@H]4CC[C@](O)(CC)[C@H](C)O4)O3)O2)[C@H](C)C[C@@H]1C
151	CHEMBL572009	C30H45N9O8	CC(C)[C@H](N)C(=O)N1CCC[C@H]1C(=O)N[C@H](C(=O)N1CCC[C@H]1C(=O)Nc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@@H]1O)C(C)C
152	CHEMBL1970547	C35H52N10O10	CCOC(=O)NC(=O)c1cn(CCN2CCN(C(=O)CCCCCCCCCCNc3ncnc4c3ncn4C3OC(CO)C(O)C3O)CC2)c(=O)[nH]c1=O
153	CHEMBL610667	C25H34N10O8	OC[C@@H]1OC(n2cnc3c(NCCCCCNc4ncnc5c4ncn5C4O[C@H](CO)[C@@H](O)[C@H]4O)ncnc32)[C@@H](O)[C@H]1O
154	CHEMBL3629350	C27H33N7O11S	NC(=O)c1csc([C@@H]2O[C@H](COC(=O)[C@H]3CCCC[C@@H]3C(=O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)[C@H](O)[C@@H]3O)[C@@H](O)[C@H]2O)n1

155	CHEMBL3629351	C27H33N7O11S	NC(=O)c1csc([C@@H]2O[C@H](COC(=O)[C@@H]3CCCC[C@H]3C(=O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)[C@H](O)[C@@H]3O)[C@@H](O)[C@H]2O)n1
156	CHEMBL2003101	C22H27N11O6	Cc1cn(C2CC(N/C(=N/C#N)NCC3OC(n4cnc5c(N)ncnc54)CC3O)C(CO)O2)c(=O)[nH]c1=O
157	CHEMBL3315299	C40H56N10O14	CC(=O)N[C@H]1[C@@H](OCc2ccccc2)O[C@H](CO)[C@@H](O)[C@@H]1O[C@H](C)C(=O)N1CCC[C@@H]1C(=O)N[C@H](CCC(=O)NCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C(N)=O
158	CHEMBL3315304	C39H54N10O14	CC(=O)N[C@H]1[C@@H](OCc2ccccc2)O[C@H](CO)[C@@H](O)[C@@H]1OCC(=O)N1CCC[C@@H]1C(=O)N[C@H](CCC(=O)NCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C(N)=O
159	CHEMBL3357336	C21H28N10O4S	Nc1ncnc2c1ncn2[C@@H]1O[C@H](Cn2cc(CCCC[C@@H]3SC[C@@H]4NC(=O)N[C@@H]43)nn2)[C@@H](O)[C@H]1O
160	CHEMBL3770986	C25H31FN6O3S	CN1[C@@H]2CCC[C@H]1C[C@@H](Nc1ncnc3c1ncn3[C@@H]1O[C@H](CSc3ccccc3F)[C@@H](O)[C@H]1O)C2
161	CHEMBL4107217	C27H33F3N8O4	CC(C)N(C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)[C@H]1C[C@H](CCc2nc3cc(OC(F)(F)F)ccc3[nH]2)C1
162	CHEMBL4108783	C27H33F3N8O4	CC(C)N(C[C@H]1O[C@@H](n2cnc3c(N)ncnc32)[C@H](O)[C@@H]1O)[C@H]1C[C@@H](CCc2nc3cc(OC(F)(F)F)ccc3[nH]2)C1
163	CHEMBL1164549	C23H33N7O10	O=C(NCc1cn(C[C@H]2O[C@@H](OC[C@H]3O[C@@H](Cn4ccc(=O)[nH]c4=O)[C@@H](O)[C@@H]3O)[C@H](O)[C@@H]2O)nn1)[C@@H]1CCCN1
164	CHEMBL4106621	C31H43N7O3	CC(C)N(C[C@H]1O[C@@H](n2ccc3c(N)ncnc32)[C@H](O)[C@@H]1O)[C@H]1C[C@H](CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1

165	CHEMBL4114909	C29H39N7O3	CN(C[C@H]1O[C@@H](n2ccc3c(N)ncnc32)[C@H](O)[C@@H]1O)[C@H]1C[C@@H](CCc2nc3cc(C(C)(C)C)ccc3[nH]2)C1
166	CHEMBL1643128	C29H33N7O5	Cc1cn([C@H]2C[C@H](n3cc(C4CN5CCC4C[C@@H]5[C@@H](O)c4ccnc5ccccc45)nn3)[C@@H](CO)O2)c(=O)[nH]c1=O
167	CHEMBL1092022	C26H41ClN11O9P	Cl.N=C(N)NCCCCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
168	CHEMBL1198939	C26H40N11O9P	N=C(N)NCCCCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
169	CHEMBL251708	C31H46N6O6	CC(C)(C)c1cc(C(=O)NCCCCCCNc2ncnc3c2ncn3[C@@H]2O[C@H](CO)[C@@H](O)[C@H]2O)cc(C(C)(C)C)c1O
170	CHEMBL273846	C27H31N5O7	CN(C)c1ccc(C2CC(=O)C3C(C2)OC(N)=C(C#N)C3c2cn([C@@H]3C[C@@H](O)[C@H](CO)O3)c(=O)[nH]c2=O)cc1
171	CHEMBL1928285	C26H36N12O5S	CC1(C)Nc2nc(N)[nH]c(=O)c2N=C1C(=O)NCCN1CCC(SC[C@H]2O[C@@H](n3cnc4c(N)ncnc43)[C@H](O)[C@@H]2O)CC1
172	CHEMBL357055	C21H30N6O5S	O[C@@H]1[C@@H](CO/C(S)=N/C2CCCCC2)OC(n2cnc3c(NC4CCOC4)ncnc32)[C@@H]1O
173	CHEMBL4107547	C28H34F3N7O4	CC(C)N(C[C@H]1O[C@@H](n2ccc3c(N)ncnc32)[C@H](O)[C@@H]1O)[C@H]1C[C@@H](CCc2nc3cc(OC(F)(F)F)ccc3[nH]2)C1
174	CHEMBL1092019	C24H36N9O9P	NCCCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
175	CHEMBL1877814	C23H30N6O9	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CNCc2ccccc2OC2OC(CO)C(O)C(O)C2O)[C@@H](O)[C@H]1O
176	CHEMBL4471176	C41H60N6O11	CO/C1=C\CC(=O)O[C@H](C)C/C=C/C=C/[C@H](O[C@H]2CC[C@H](N(C)C)[C@@H](C)O2)[C@H](C)C[C@@H]2

			C[C@H](OCc3cn([C@H]4C[C@H](n5cc(C)c(=O)[nH]c5=O)O[C@@H]4CO)nn3)O[C@@H]12
177	CHEMBL610666	C25H36N12O8	Nc1nc(NCCCCCNc2nc(N)nc3c2ncn3C2O[C@H](CO)[C@@H](O)[C@H]2O)c2ncn(C3O[C@@H](CO)[C@H](O)[C@@H]3O)c2n1
178	CHEMBL3614055	C20H28N12O6S2	[N-]=[N+]=N[C@@H]1[C@H](O)[C@@H](CNS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)O[C@H]1n1cnc2c(N)ncnc21
179	CHEMBL3614057	C20H28N12O6S2	[N-]=[N+]=N[C@H]1[C@H](O)[C@@H](CNS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)O[C@H]1n1cnc2c(N)ncnc21
180	CHEMBL3614058	C20H28FN9O6S2	Nc1ncnc2c1ncn2[C@@H]1O[C@H](CNS(=O)(=O)NC(=O)CCCC[C@@H]2SC[C@@H]3NC(=O)N[C@@H]32)[C@@H](O)[C@H]1F
181	CHEMBL3681915	C23H26N10O8	Nc1ncnc2c1ncn2[C@@H]1O[C@H](COCC#Cc2nc3c(N)ncnc3n2[C@@H]2O[C@H](CO)C(O)[C@@H]2O)C(O)[C@@H]1O
182	CHEMBL3590176	C32H49N9O20	OC[C@H]1O[C@@H](OCc2cn([C@H]3[C@H](O)[C@@H](O)[C@H](n4cc([C@@H]5O[C@H](CO)[C@@H](n6cc(CO[C@@H]7O[C@H](CO)[C@H](O)[C@H](O)[C@H]7O)nn6)[C@H](O)[C@H]5O)nn4)O[C@@H]3CO)nn2)[C@H](O)[C@@H](O)[C@H]1O
183	CHEMBL1092017	C22H32N9O9P	NCCCNc1ccn([C@H]2C[C@H](OP(=O)(O)OC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)C[C@@H]3O)[C@@H](CO)O2)c(=O)n1
184	CHEMBL3220561	C34H66N8O8	CCCCCCCCCCCCCCc1cn(C[C@H]2O[C@H](O[C@@H]3[C@@H](O)[C@H](O[C@H]4O[C@H](CN)[C@@H](O)C[C@H]4N)[C@@H](N)C[C@H]3N)[C@H](O)[C@@H](N)[C@@H]2O)nn1

185	CHEMBL3220800	C32H62N8O8	CCCCCCCCCCCCc1cn(C[C@H]2O[C@H](O[C@@H]3[C@@H](O)[C@H](O[C@H]4O[C@H](CN)[C@@H](O)C[C@H]4N)[C@@H](N)C[C@H]3N)[C@H](O)[C@@H](N)[C@@H]2O)nn1
186	CHEMBL509955	C23H40N6O12S	NC[C@H]1O[C@@H](OC[C@H]2O[C@@H](OCCSC[C@H]3O[C@@H](n4ccc(N)nc4=O)[C@H](O)[C@@H]3O)[C@H](N)[C@@H](O)[C@@H]2O)[C@H](N)[C@@H](O)[C@@H]1O
187	CHEMBL508103	C20H27N9O11S3	NC(=O)c1csc([C@@H]2O[C@H](CNS(=O)(=O)CS(=O)(=O)NC[C@H]3O[C@@H](n4cnc5c(N)ncnc54)[C@H](O)[C@@H]3O)[C@@H](O)[C@H]2O)n1
188	CHEMBL1683750	C20H27N9O11S3	NC(=O)c1csc([C@@H]2O[C@H](CNS(=O)(=O)CS(=O)(=O)NC[C@@H]3O[C@H](n4cnc5c(N)ncnc54)[C@@H](O)[C@H]3O)[C@@H](O)[C@H]2O)n1
189	CHEMBL1162399	C24H41N11O9	NC[C@H]1O[C@H](O[C@H]2[C@@H](NCCNC(=O)[C@H]3O[C@@H](n4cnc5c(N)ncnc54)[C@H](O)[C@@H]3O)[C@@H](O)[C@H](N)C[C@@H]2N)[C@H](N)[C@@H](O)[C@@H]1O
190	CHEMBL4112163	C25H33N7O5S	NC(=O)CNCC1CCN(c2nc(N[C@@H]3C[C@H](CO)[C@@H](O)[C@H]3O)c(c3nc4ccccc4s3)c(=O)[nH]2)CC1
191	CHEMBL3315298	C39H56N10O15	CC[C@@H](NC(=O)[C@@H](C)O[C@H]1[C@H](O)[C@@H](CO)O[C@H](OCc2ccccc2)[C@@H]1NC(C)=O)C(=O)N[C@H](CCC(=O)NCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C(N)=O
192	CHEMBL3315306	C39H56N10O14	CC(=O)N[C@H]1[C@@H](OCc2ccccc2)O[C@H](CO)[C@@H](O)[C@@H]1OCC(=O)N[C@@H](C(=O)N[C@H](CCC(=O)NCCNc1ncnc2c1ncn2[C@@H]1O[C@H](CO)[C@@H](O)[C@H]1O)C(N)=O)C(C)C
193	CHEMBL3953205	C23H32N8O6S	NS(=O)(=O)OC[C@H]1O[C@@H](n2cnc3c(NCCN4CCN(Cc5ccccc5)CC4)ncnc32)[C@H](O)[C@@H]1O
194	CHEMBL3769861	C22H33N7O4	CCNC(=O)[C@H]1O[C@@H](n2cnc3c(N4[C@@H]5CCC[C@H]4C[C@H](N(C

			)C)C5)ncnc32)[C@H](O)[C@@H]1O
195	CHEMBL609820	C23H26N6O4S2	COc1ccc2nc(SC[C@H]3OC(n4cnc5c(NC6CCCC6)ncnc54)[C@H](O)[C@@H]3O)sc2c1
196	CHEMBL1643130	C33H39N7O6	C=CC1CN2CCC1C[C@@H]2[C@@H](OCc1cn([C@H]2C[C@H](n3cc(C)c(=O)[nH]c3=O)O[C@@H]2CO)nn1)c1ccnc2ccc(OC)cc12
197	CHEMBL1643129	C33H39N7O6	C=CC1CN2CCC1C[C@H]2[C@H](OCc1cn([C@H]2C[C@H](n3cc(C)c(=O)[nH]c3=O)O[C@@H]2CO)nn1)c1ccnc2ccc(OC)cc12
198	CHEMBL4464507	C22H26N14O6	Nc1ncnc2c1ncn2[C@@H]1O[C@@H]2CNC(=O)N[C@H]3[C@@H](O)[C@H](n4cnc5c(N)ncnc54)O[C@@H]3CNC(=O)N[C@H]2[C@H]1O
199	CHEMBL609532	C23H26N6O4S2	COc1ccc2sc(SC[C@H]3OC(n4cnc5c(NC6CCCC6)ncnc54)[C@H](O)[C@@H]3O)nc2c1
200	CHEMBL1983079	C37H62N5O12P	CCCCCCCCCCCCCCCCCCCCNc1ccn(C2OC(COP(=O)(O)OCC3OC(n4cc(C)c(=O)[nH]c4=O)CC3O)C(O)C2O)c(=O)n1

Table 1: LIST OF 200 INHIBITIRS FROM CHEMBL DATABASE

Molecular Docking:

"Molecular docking" is a widely used computer technique that predicts and analyzes the binding mechanism and affinity of tiny molecules (ligands) to target proteins or macromolecular structures. Drug discovery and structural biology both make use of it. It entails determining both the energetics and the spatial arrangement of the ligand within the protein binding site. Molecular docking is a vital tool in the quest for novel therapeutic opportunities because of its capacity to measure binding affinities, quantify the intensity of ligand-protein interactions, and evaluate binding poses. By providing insights into the structural basis of ligand-receptor interactions, molecular docking aids in the design and optimization of new therapeutic medications. (Trott & Associates, 2010)

Multiple molecule docking was carried out using a variety of docking software and sites, and the binding energy (Kcal/Mol) of the different software was compared. Using molecular docking with ARGUS LAB, CB-DOCK, and AUTODOCK, the lowest binding energy of the ligand interacting with the protein was found.

Argus Lab Docking:

Docking is made easier by Argus Lab, a program for drug creation and molecular modeling that follows a methodical procedure. The software is first launched, and receptor and ligand structures are loaded in the proper file formats. Optimizing the receptor's structure, modifying its protonation states, and fixing any problems will prepare it. In a similar vein, incorporate hydrogen atoms to improve the ligand structure. Specify the scoring functions and the search space for the docking parameters. Start the

docking computation so that Argus Lab can investigate possible binding modes. Determine binding locations and interactions by analyzing the data. Use molecular graphics to visualize the results and adjust the parameters as necessary to ensure accuracy. Save the outcomes, then create reports that include a summary of the top binding positions and scores.

Using Argus Lab, 200 ligands found through target-based screening were docked with the Hsp90 protein in a thorough docking analysis. This thorough technique offers important insights into the possible interactions between the ligands and the Hsp90 protein, supporting efforts in drug discovery and design. The highest Argus Lab score recorded was -9.85 kcal/mol.

CB-Docking:

Ten spike protein ligands, ten protease protein ligands, and ten ACE2 receptor ligands were used for CB-DOCK docking. It's an internet docking platform. Online docking, also known as web-based docking, allows molecular docking investigations to be conducted remotely through a computer interface. It provides researchers with docking tools and resources without forcing them to install specialized software or perform time-consuming calculations locally. Online docking platforms provide user-friendly interfaces that facilitate the setup of docking studies, submission of protein and ligand structures, and display of docking results. In order to predict the ligand and receptor binding affinities and modalities, these platforms often employ robust docking algorithms and scoring systems.

Because online docking systems are more user-friendly, accessible, and have a larger user base, they promote collaborative research and speed up drug discovery initiatives.

Swiss Dock:

The design and development of drugs heavily relies on protein-ligand docking modeling. Consequently, it is crucial to design web servers meant for docking simulations. A web server called SwissDock is devoted to doing protein-ligand docking simulation in an elegant and user-friendly manner. SwissDock offers an easy-to-use, integrated interface and is based on the protein-ligand docking tool EADock DSS. The SwissDock sends back the results via email and lets the user upload structural files for both ligands and proteins. We can use the UCSF Chimera tool to prepare these input files, which will make it easier to upload the protein and ligand files. This chapter explains how to simulate protein-ligand docking using UCSF Chimera and SwissDock.

S.NO	LIGAND ID	CB DOCK SCORE	ARGUS LAB	SWISS DOCK	AUTO-DOCK
1	CHEMBL3769408	-8.4	-8.1	-8.47	-9.55
2	CHEMBL4209821	-9.3	-8.73	-8.62	-9.55
3	CHEMBL608748	-9.3	-8.2	-8.58	-8.89
4	CHEMBL3679378	-9.6	-8.68	-9.23	-9.47
5	CHEMBL3679385	-9.7	-8.13	-8.5	-9.44
6	CHEMBL3679377	-9.5	-8.24	-8.54	-9.05
7	CHEMBL3679384	-8.6	-8.02	-8.77	-8.64
8	CHEMBL338399	-6.8	-7.67	-9.64	-9.32
9	CHEMBL1823453	-9.3	-8.14	-11.04	-9.44
10	CHEMBL612210	-8.7	-7.54	-8.6	-8.15
11	CHEMBL2112632	-7.9	-8.81	-7.68	-9.38
12	CHEMBL391031	-9.6	-7.78	-8.37	-8.16

13	CHEMBL2147151	-8.7	-8.76	-9.41	-9.62
14	CHEMBL610983	-9	-7.62	-8.88	-8.44
15	CHEMBL55099	-9.9	-8.95	-9.87	-10.06
16	CHEMBL2364571	-9.1	-7.88	-7.75	-8.34
17	CHEMBL2112106	-9.3	-7.67	-9.07	-8.24
18	CHEMBL2112185	-8.3	-8.08	-8.2	-8.51
19	CHEMBL2364570	-9.2	-7.58	-7.92	-8.62
20	CHEMBL4095344	-9.3	-8.49	-8.85	-10.43
21	CHEMBL2071119	-8.8	-8.23	-9.48	-5.33
22	CHEMBL3679379	-9.2	-9.85	-9.21	-9.25
23	CHEMBL3674590	-9.2	-8.55	-8.97	-9.21

Table 2 : ADMET & Ro5 SCREENED LIGANDS

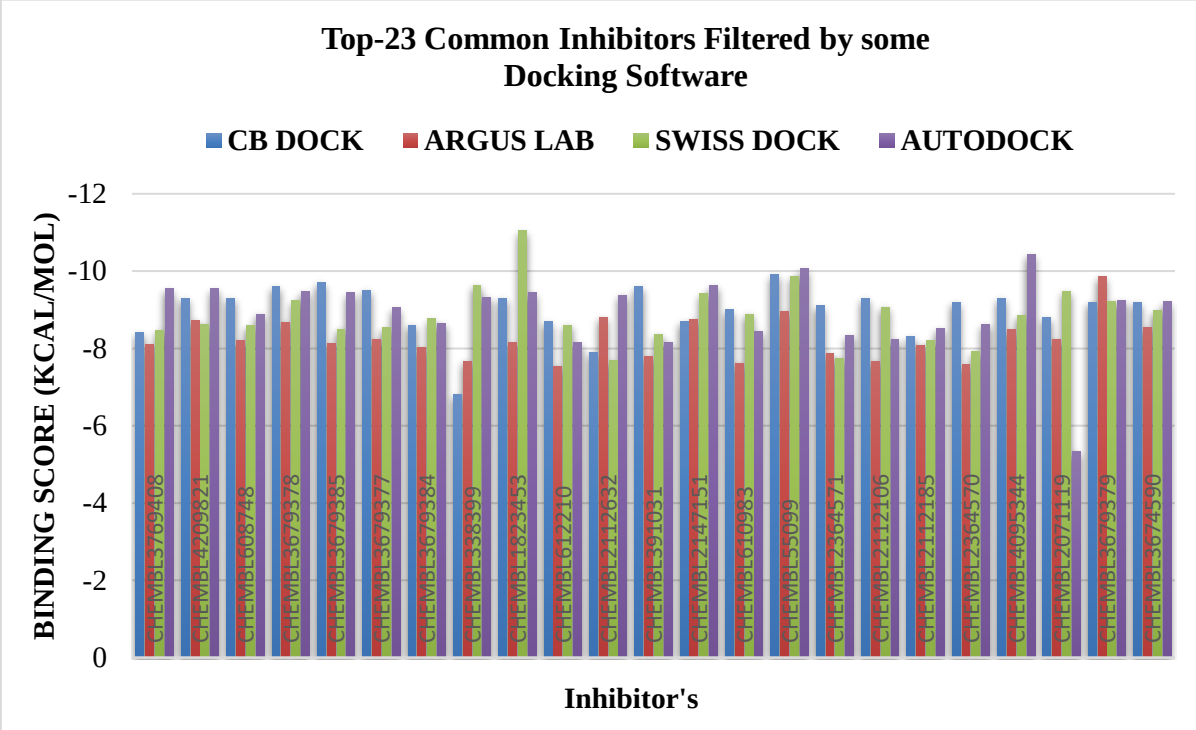

Fig. 02 : Histogram of Top-23 Compound

Hsp90 Protein:

Following the conclusion of the docking study by Argus Lab, ligands surpassing the energy binding score threshold of >= -10 kcal/mol were chosen using a selective filtering procedure. After this thorough screening, a subset of 23 ligands was identified, and AutoDock 4.0 was used to conduct additional docking studies on these ligands. The goal of this phase was to refine the selection based on higher binding energy scores. Notably, all seven of the top ligands showed remarkable values that exceeded -9.0 kcal/mol.

CB-Dock-2 with top 23 ligands:

Subsequent to the Auto Dock 4.0 analyses, further molecular docking studies were conducted using CB-Dock 2, focusing on Hsp90. CB-Dock 2 systematically explored the binding interactions of the

previously identified top 10 ligands showing highest binding scores with these proteins. The comprehensive analysis aimed to provide insights into the potential inhibitory effects of the ligands on critical viral protein. This multi-protein evaluation through CB-Dock 2 contributes to a holistic understanding of the ligands' binding affinities and offers valuable information for developing targeted therapeutic strategies against Hsp90 protein.

3D Structure Retrieval, Preparation, and Energy Minimization of Hsp90:

Hsp90 protein:

The RCSB PDB database provided the crystal structure of the Hsp90 protein (PDB ID: 2CVJ) at a resolution of 2.00 Å. In order to get the protein ready for docking analysis, heteroatoms, ions, and superfluous molecules were removed from the protein's apo form using BIOVIA Discovery Studio. Swiss PDB viewer was used to minimize energy in order to improve the Hsp90 protein's structural integrity and conformational stability. Refining the protein structure reduces energy by reducing unfavourable interactions and stabilizing the molecule. The goal was to obtain a more accurate depiction of the spike protein's natural state for use in later computer analysis. This procedure guarantees that the protein structure is optimized and appropriate for additional research, including molecular docking experiments.

Target based virtual screening:

Target-based virtual screening of the Hsp90 protein has emerged as a key strategy in the hunt for putative cancer therapy inhibitors. Scholars have utilized diverse computational techniques to ascertain highly effective chemicals possessing anti-tumor properties. Structure-based virtual screening finds compounds with high binding affinity and specificity by screening compound libraries using the three-dimensional structure of the Hsp90 protein. By offering insights into the binding mechanisms and directing the development of inhibitor design, molecular dynamics simulations are essential in forecasting the stability and interactions of Hsp90-inhibitor complexes. Validating the computational predictions and determining the safety and effectiveness of the identified inhibitors require experimental testing through in vitro and in vivo biological studies. The drug discovery process has been sped up by the development of machine learning algorithms, which have further improved screening efficiency and accuracy, By concentrating on the structural characteristics and chemical characteristics of recognized Hsp90 inhibitors, ligand-based virtual screening broadens the pool of viable candidates and enhances the structure-based method. Fascinatingly, scientists have also investigated novel chemical scaffolds with therapeutic potential for the treatment of cancer by virtually screening substances derived from the sea. Promising inhibitors with important implications for cancer therapy have been found by the combination of computational tools, experimental validations, and creative approaches in target-based virtual screening of the Hsp90 protein.

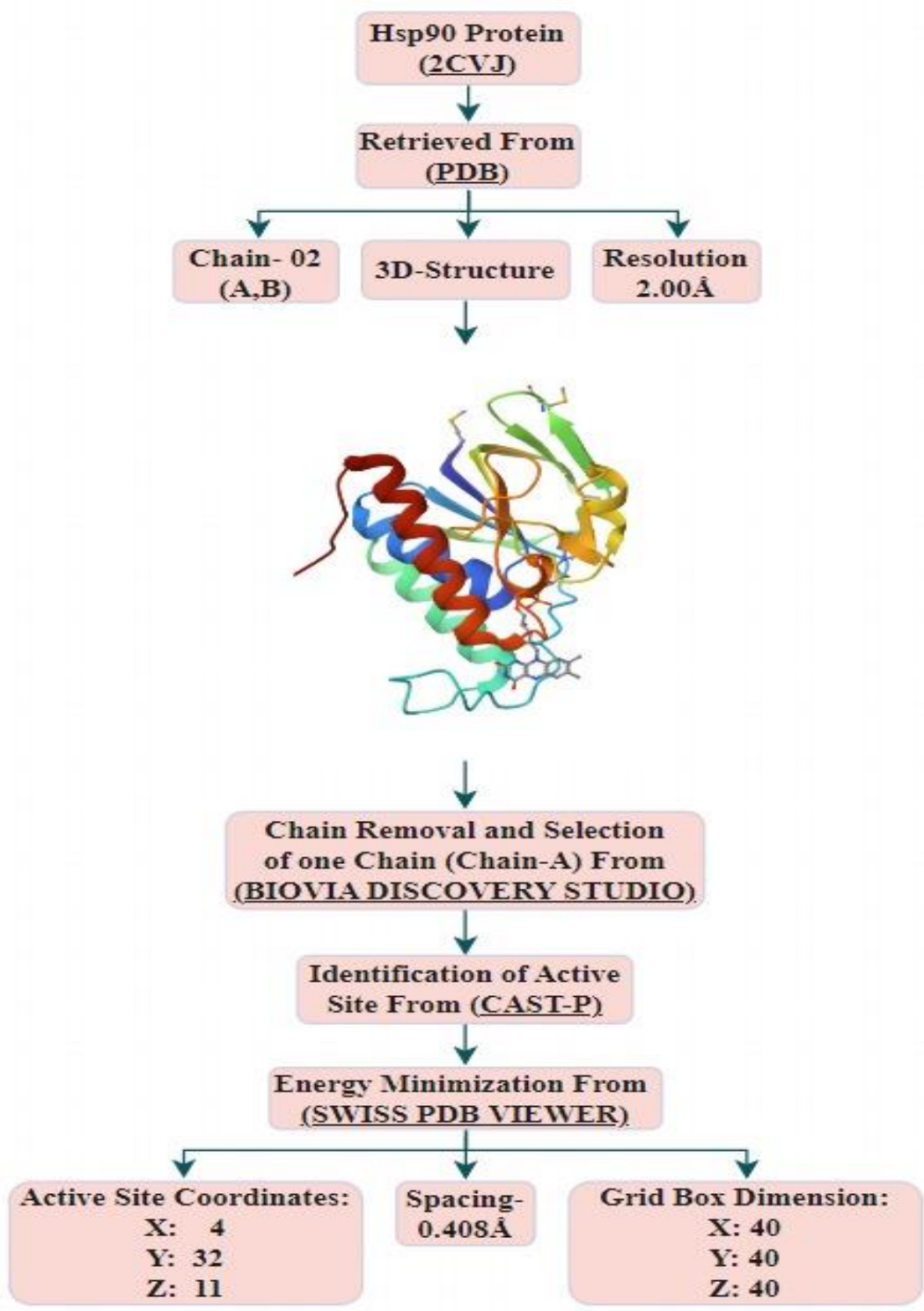

Fig. 03 : Flow Chart of Hsp90 Protein

Result & Discussion:

Receptor based Screening Analysis Based on Targets:

Swiss ADME research was conducted on a ligand library comprising Pharmacophore, and results indicated that 23 compounds had favourable ADME properties. Based on their distinguishing features, including optimal permeability of the blood-brain barrier (BBB) and optimal absorption of the human

intestinal tract (HIA), these potential candidates were selected through the use of Target-Based Screening (TBS). Ghose, Veber, Egan, and Muegge factors, along with Lipinski's Rule of Five (RO5), were additional assessments that demonstrated the similarity of their medicinal products. This rigorous evaluation demonstrates the attempt to identify compounds with good ADME characteristics, which raises the possibility that these compounds may be successfully converted into beneficial medicinal therapies.

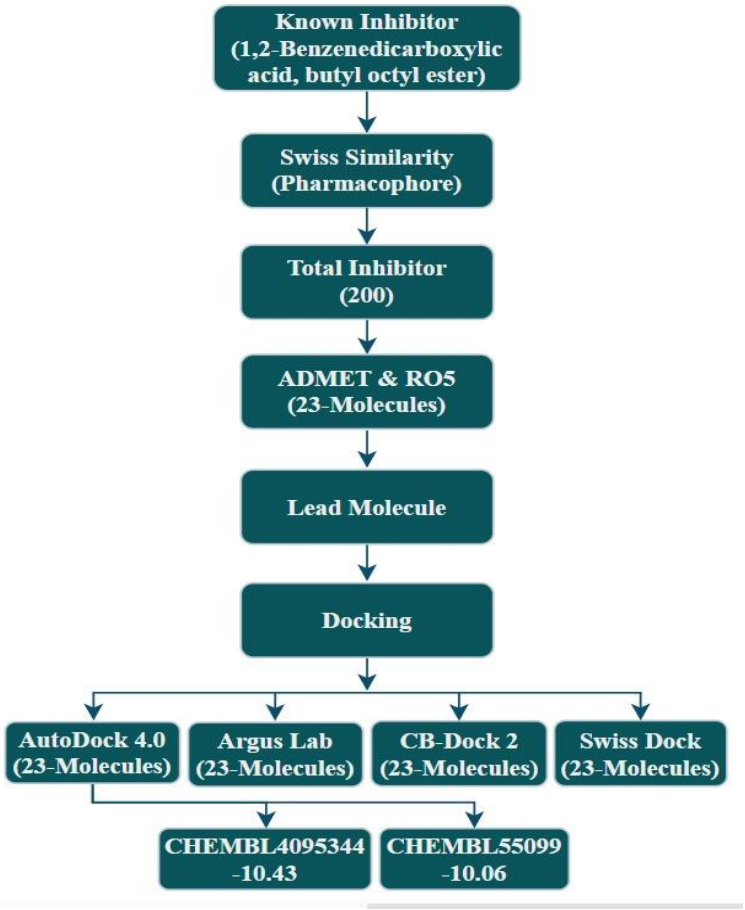

Fig. 04 : Flow chart of retrieving inhibitors of Hsp90 Protein

The following are the complexes from the docking of the top analogs and modified analogs

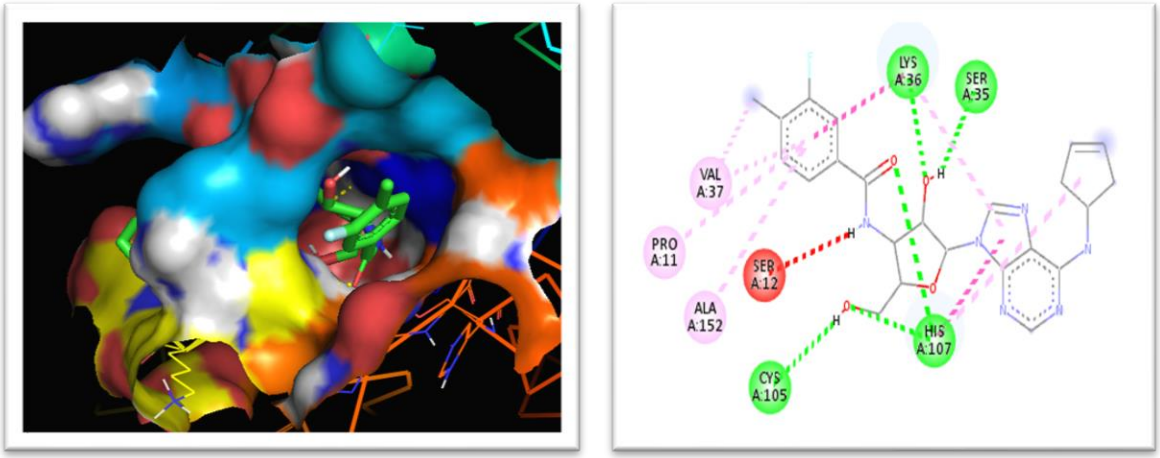

Fig. 05 : 2D & 3D structure of CHEMBL55099

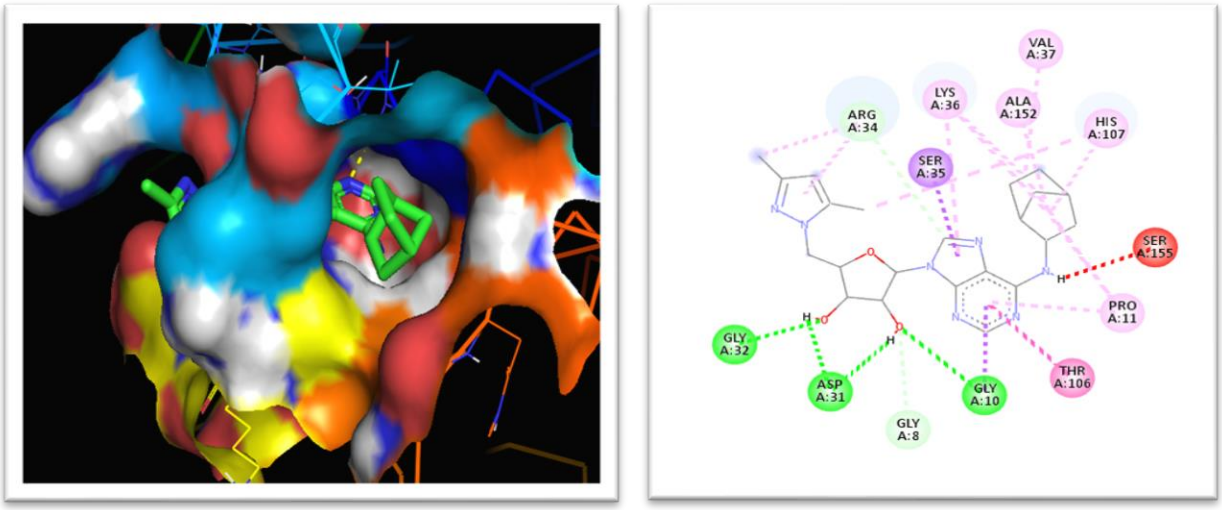

Fig.06 : 2D & 3D structure of CHEMBL4095344

CONCLUSION

The analogue with the best Delta G value was ultimately determined by all of the docking results, and since its pharmacophore kinetics analysis and RO5 analysis show that it has good biological properties, we can conclude that it is the best candidate to act as an inhibitor for the Hsp90 mutation.

From various screening methodologies and docking techniques we are able to deduce that the top analogs CHEMBL55099 & CHEMBL4095344 are best candidates for being a possible hit then upon modification of said analogs we were able to further improve overall biological activity and essentially design a novel drug molecule that has desirable affinity toward the target protein and desirable biological activity as well however upon further analysis the best analog to inhibit the mutation of Hsp90 protein is CHEMBL4095344 since it has more favorable attributes which makes it the best potential hit molecule that combat against the mutation of Hsp90 protein.

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