Supplementary Table 1 : Exact sources and number of molecules from various virtual libraries

Library	**Filters applied**	**No of molecules**	**Downloaded date (sdf format)**
ZINC	for-sale+in-trials+fda+in-man+in-cells+in-vivo+in-vitro+world	500	13-4-2023 and 17-4-2023
NCI	Nil	34580	24-4-2023
CHembridge	Nil	1780	24-4-2023
Life Chemicals	Anticancer Focused Library by 2D Similarity Search and Anticancer Targeted Library by Docking	13,600	5-4-2023
LifeChemicals	Biologically Active Compound Library and Natural Product-like Compound Libraries and PPI Focused Libraries by Ligand-based Approach	77,332	5-4-2023
ChemDB	Nil	54	20-4-2023
Total		**127,846**	

Supplementary Table 2: **Presents the top five compounds along with their SMILES format**

Sl no	Small molecule	SMILES
1.	Cefotetan	NC(=O)C(C([O-])=O)=C1S[C@@H](S1)C(=O)N[C@]2(OC)C(=O)N([C@@H]23)C(C([O-])=O)=C(CS3)CSc4nnnn4C
2.	F0922-0590	COc(cc1)c(OC)cc1CCNC(=O)c2ccc(cc2)Cn(c3=O)c(=O)n(c(c34)cccc4)Cc5c(C)ccc(C)c5
3.	F0385-0029	[O-]C(=O)c1cc(ccc1)NC(=O)CCCN(C(=S)S2)C(=O)/C2=C3\C(=O)N(C(=S)S3)CCCC(=O)Nc(cc4C([O-])=O)ccc4
4.	F6658-4634	n1cnn(c12)c(c(C)c(n2)C)N3CCN(CC3)c4cc(=O)n(C)c(=O)[nH]4
5.	2,6,7-trihydroxy-9-(2-hydroxyphenyl)-3H-xanthen-3-one	c1cccc(O)c1-c2c(cc(O)c(c3)O)c3oc(c24)cc(=O)c(c4)O

Supplementary Table 3: **Molecules after each stage of docking from various libraries**

Sl no	**Database**	**Number of molecules**	**After HTVS**	**After SP**	**After XP**	**After MMGBSA**
1	ZINC	500	748	30	22	22
2	LifeChemicals	13,600(2 sim and docking) 77,332(rest)	14433(2d sim) 2763(docking) 105435(rest)	14420 2D sim(898) 144(docking) 3005(rest)	945(2D sim) 111(docking) 2001(rest)	278(2dsim) 24(docking) 372(rest)
3	Chembridge	1780	3900	160	122	33
4	NCI	34580	1269	838	629	226
5	ChemdB	54	--	--	54	54

Supplementary Material 1 : Details of ZDOCK protocol

The PDB ids 1HCN (for human chorionic gonadotropin) and 1PLO (for TGFβR-II) were entered at the https://www.rcsb.org/ website and the structures were downloaded and viewed in Pymol. For 1PLO, several models were available and only the first model was chosen to be loaded in ZDOCK, and the other models were deleted before saving under the name 1PLO.pdb. Similarly, for 1HCN the alpha chain was deleted and saved as 1HCN.pdb as crystal structure of β-hCG was not available. These modified pdb ids were loaded in ZDOCK with 1HCN loaded first as this was the larger file. The "Skip residue selection" option was chosen and then submitted. The results were then obtained via email after which a diagrammatic representation was made of the top 10 models of β-hCG with binding sites of TGFβR-II in red with rectangles indicates indicating the frequency of occurrence of these residues. Please find below the details of the sequences submitted to ZDOCK

ZDOCK complex sequence

TGFβR-II

VTDNNGAVKFPQLCKFCDVRFSTCDNQKSCMSNCSITSICEKPQEVCVAVWRKNDENITLET
VCHDPKLPYHDFILEDAASPKCIMKEKKKPGETFFMCSCSSDECNDNIIFSEEYNTSNPD

β-hCG

KEPLRPRCRPINATLAVEKEGCPVCITVNTTICAGYCPTMTRVLQGVLPALPQVVCNYRDVRF
ESIRLPGCPRGVNPVVSYAVALSCQCALCRRSTTDCGGPKDHPLTCD

Supplementary Material 2 : Details of MD simulation and Ligand preparation

MD simulation parameters

Simulation time set : 100 ns
Ensemble : NPT
Temperature : 300 K

Ligand preparation details

The LigPrep module in Schrödinger package is used in the comprehensive ligand preparation process that generates a high-quality library for virtual screening and docking studies. The process involves several key steps, including expanding tautomeric and ionization states, generating ring conformations, producing stereoisomers, and performing structural optimization. Tautomers arise from proton relocations within the molecule and are predicted using knowledge-based rules and the Epik module. Ionization states are generated using the Epik module, which calculates pKa values for ionizable groups and generates appropriate states within a user-defined pH range.

LigPrep also generates ring conformations by exploring low-energy ring geometries and ensuring compatibility with the active site of the receptor in docking simulations. It also produces stereoisomers for ligands with chiral centers to account for enantiomers and diastereomers, accommodating the possibility of receptor-specific enantioselectivity or diastereoselectivity.

Structural optimization is performed using the OPLS4 force field to ensure the prepared ligands are chemically accurate and energetically favorable. Filtering and refinement are also possible, with the output filtered based on physicochemical properties and user-defined parameters, such as the number of tautomers, stereoisomers, or ring conformations per compound.