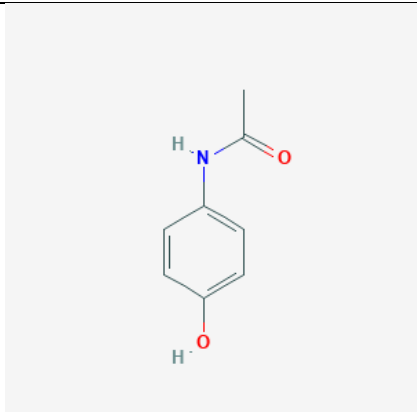
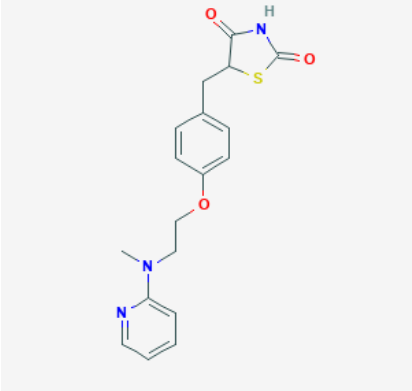
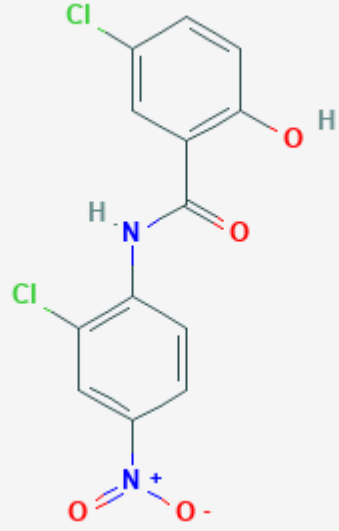


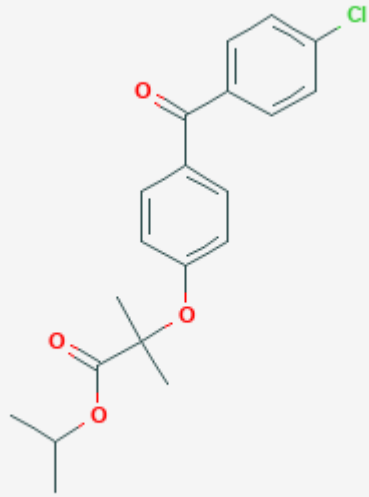
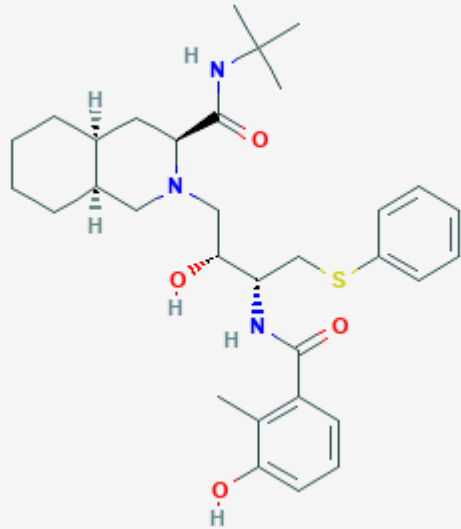
An Up-to-date Overview of Computational Polypharmacology in Modern Drug Discovery

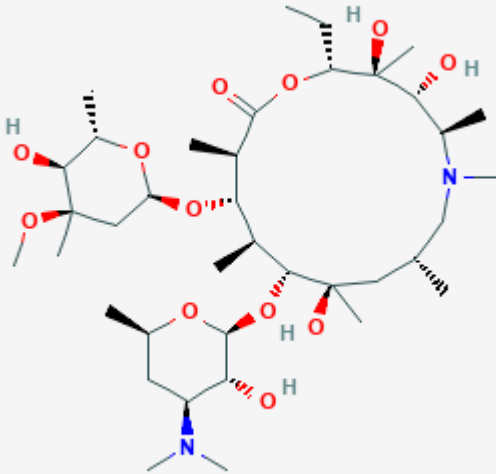
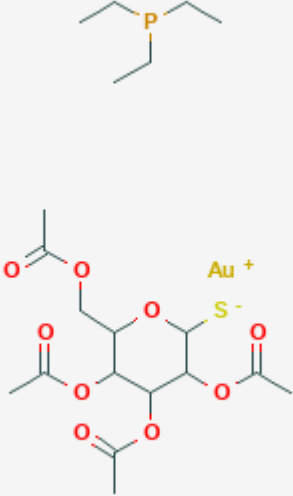
Rajan Chaudhari¹, Long Wolf Fong^{1,2}, Zhi Tan¹, Beibei Huang¹, Shuxing Zhang^{1,2,*}

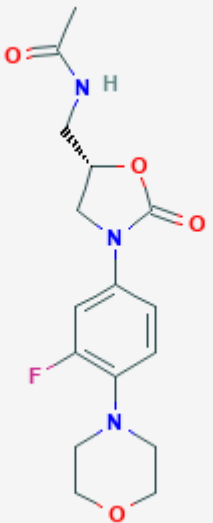
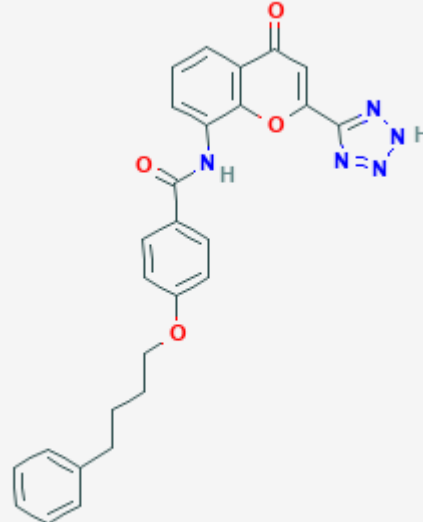
Supplementary Table 3.1: Chemical structures and physicochemical properties of repurposed drugs in clinical trials.

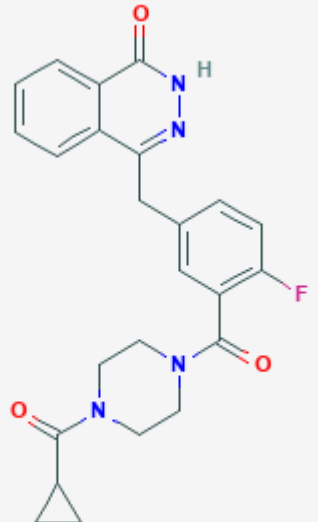
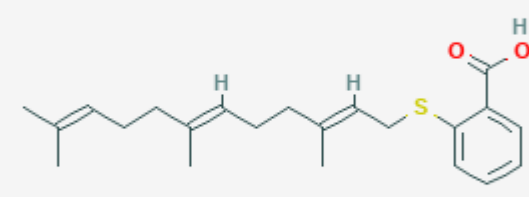
Drug Name	2D Structure	CID	Weight	TPSA	logP(o/w)	logS
Paracetamol/Acetaminophen	 The image shows the 2D chemical structure of Paracetamol (Acetaminophen). It consists of a central benzene ring. At the top position (1-position), there is an acetamido group (-NH-C(=O)-CH3). At the bottom position (4-position), there is a hydroxyl group (-OH). The nitrogen atom in the acetamido group is blue, the carbonyl oxygen is red, and the hydroxyl oxygen is red. The hydrogen atoms are shown in black.	1983	151.17	49.33	0.89	-1.23

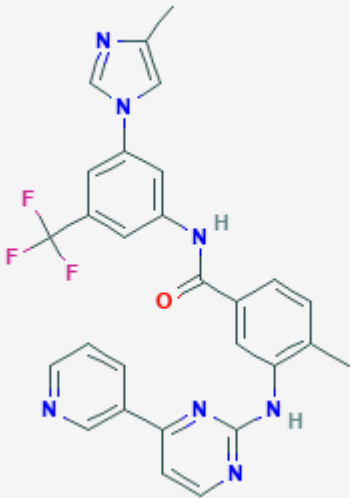
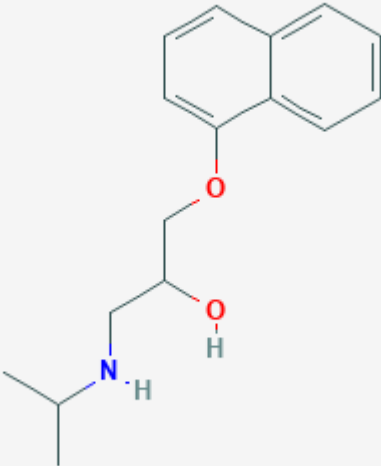
Rosiglitazone	 <p>The chemical structure of Rosiglitazone consists of a central benzene ring. At the top position, there is a propyl chain ending in a thiazolidine-4-carboxamide ring. At the bottom position, there is an ether linkage (-O-) connected to a 2-(2-dimethylaminoethyl)pyridin-5-yl group.</p>	77999	357.43	71.53	2.62	-4.00
Niclosamide	 <p>The chemical structure of Niclosamide is a symmetrical molecule. It features a central amide group (-NH-) connecting two 4-chlorophenyl rings. One of the phenyl rings is also substituted with a nitro group (-NO₂) at the para position relative to the amide linkage.</p>	4477	327.12	95.15	3.74	-5.25

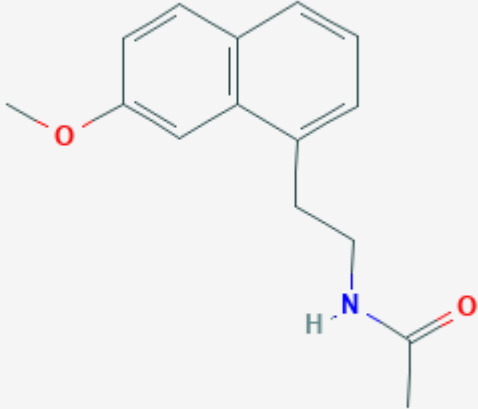
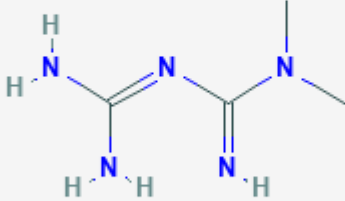
Fenofibrate	 <p>The chemical structure of Fenofibrate is shown. It consists of a central benzene ring with a chlorine atom at the para position. This ring is connected via a carbonyl group to another benzene ring. This second benzene ring is linked through an oxygen atom to a tert-butyl ester group, which is further connected to an isobutyl ester group.</p>	3339	360.84	52.60	5.16	-5.96
Nelfinavir	 <p>The chemical structure of Nelfinavir is shown. It features a complex bicyclic core with a nitrogen atom. Attached to this core are a tert-butyl amide group, a hydroxyl group, and a side chain containing a sulfur atom linked to a phenyl ring, and another nitrogen atom linked to a 2-hydroxyphenyl group.</p>	64143	567.80	101.90	5.36	-7.39

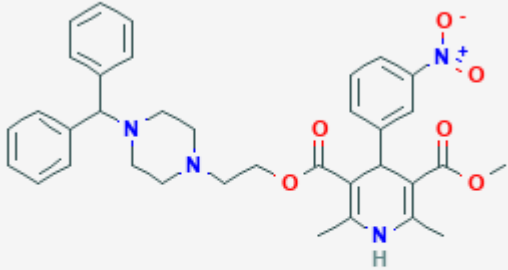
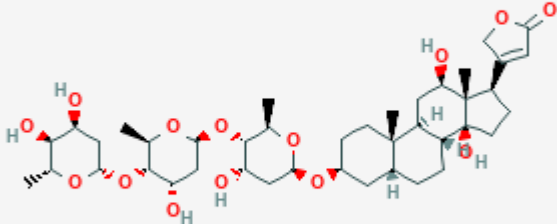
Azithromycin	 <p>The image shows the chemical structure of Azithromycin, a 15-membered macrolide antibiotic. It features a central nitrogen atom (blue) in a ring, with a methyl group (black) attached. The ring is substituted with several hydroxyl groups (red oxygen, white hydrogen) and a side chain containing a tetrahydrofuran ring and a methyl group. Stereochemistry is indicated with wedges and dashes.</p>	447043	749.00	180.08	3.43	-3.69
Tigecycline	 <p>The image shows two chemical structures related to Tigecycline. The top structure is triethylphosphine, consisting of a central phosphorus atom (orange) bonded to three ethyl groups (black). The bottom structure is the tigecycline core, a tetracycline derivative, shown as a complex polycyclic system with multiple oxygen atoms (red) and acetyl groups (black). It is coordinated to a gold ion (Au⁺, yellow) and a sulfide ion (S⁻, yellow).</p>	54686904	585.66	205.76	-0.26	-3.41

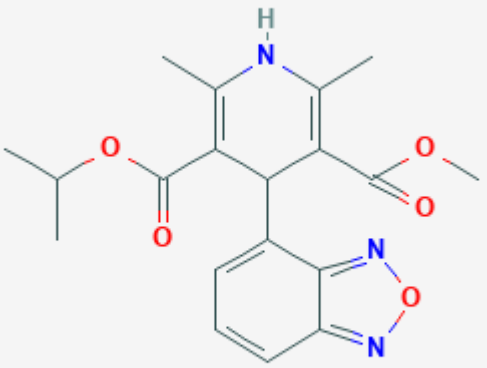
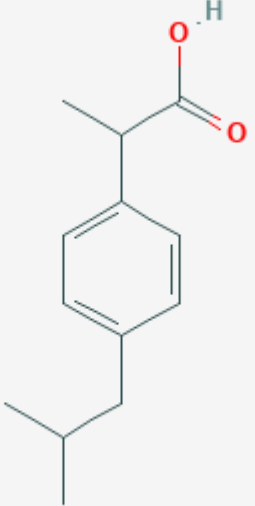
Linezolid	 <p>The chemical structure of Linezolid consists of a morpholine ring connected to a 4-fluorophenyl ring, which is further connected to a 5-membered oxazolidinone ring. A methylamino group is attached to the oxazolidinone ring.</p>	441401	337.35	71.11	0.37	-2.40
Pranlukast	 <p>The chemical structure of Pranlukast features a benzimidazole ring system. One of the benzimidazole nitrogens is substituted with a 4-(4-phenylbutoxy)phenylamino group. The other benzimidazole nitrogen is substituted with a carbonyl group.</p>	4887	481.51	119.09	4.61	-6.90

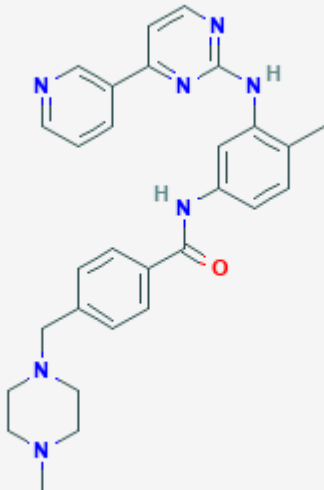
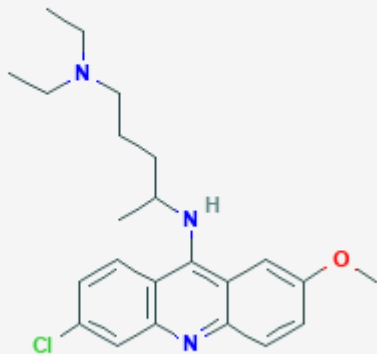
Olaparib	 <p>The image shows the chemical structure of Olaparib. It features a benzimidazole ring system with a carbonyl group at the 2-position. A methylene group connects the 4-position of the benzimidazole to a para-substituted benzene ring. This benzene ring has a fluorine atom at the 3-position and a carbonyl group at the 1-position. The carbonyl group is attached to a piperazine ring, which is further substituted with a cyclopropylmethyl group.</p>	23725625	434.47	82.08	2.53	-4.88
Salirasib	 <p>The image shows the chemical structure of Salirasib. It consists of a long, branched hydrocarbon chain with three double bonds. The chain is terminated by a sulfur atom, which is bonded to a benzene ring. The benzene ring has a carboxylic acid group (-COOH) at the 1-position and a methyl group at the 3-position.</p>	5469318	358.55	37.30	4.72	-7.24

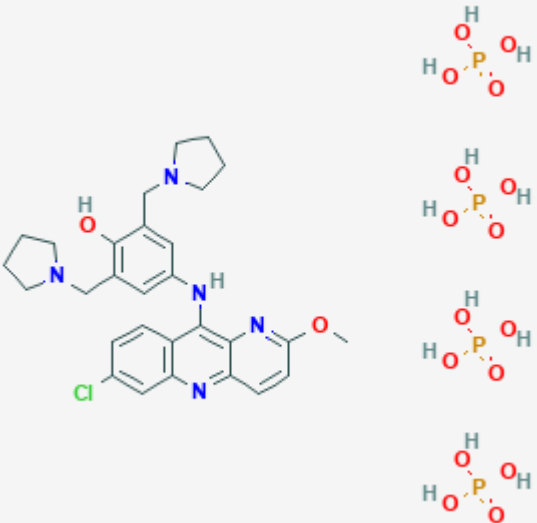
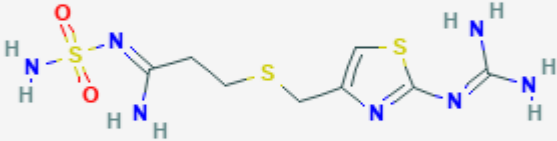
Nilotinib	 <p>The chemical structure of Nilotinib is a complex heterocyclic molecule. It features a central benzimidazole ring system. One of the benzimidazole nitrogens is substituted with a 2-methylimidazole ring. The other benzimidazole nitrogen is substituted with a 4-methylphenylamino group. The 2-position of the benzimidazole ring is substituted with a 3-(difluoromethyl)phenylamino group. The 5-position of the benzimidazole ring is substituted with a 4-pyridyl group.</p>	644241	529.53	97.62	4.34	-7.47
Propranolol	 <p>The chemical structure of Propranolol is a beta-blocker. It consists of a naphthalene ring system attached to a propanolamine chain. The naphthalene ring is connected to the chain via an ether linkage (-O-). The chain includes a secondary amine group (-NH-) and a hydroxyl group (-OH).</p>	4946	259.35	41.49	2.92	-3.53

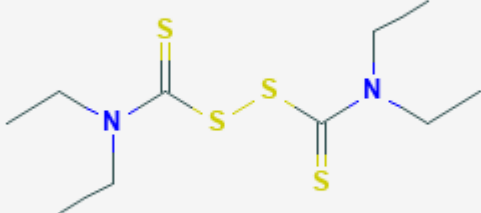
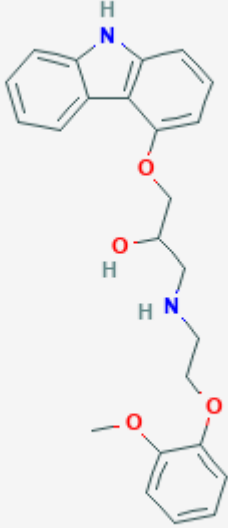
Agomelatine		82148	243.31	38.33	2.63	-3.53
Metformin		4091	129.17	91.49	-0.44	-0.23

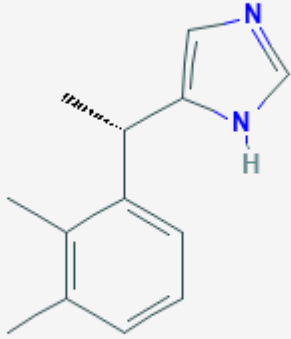
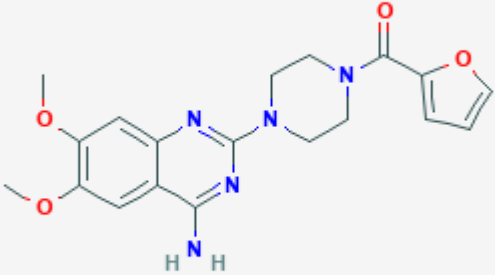
Manidipine dihydrochloride	 <p data-bbox="867 613 926 639">Cl - H</p> <p data-bbox="867 703 926 729">Cl - H</p>	150762	610.71	116.93	5.71	-7.47
Digoxin		2724385	780.95	203.06	3.32	-5.67

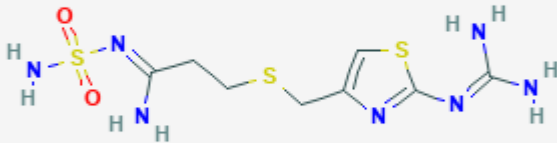

Isradipine	 <p>The chemical structure of Isradipine is a dihydropyridine derivative. It features a central dihydropyridine ring with a hydrogen atom on the nitrogen atom. The ring is substituted with two methyl groups at the 2 and 6 positions. At the 4 position, there is a 1,2,4-benzoxazin-3-yl group. At the 3 position, there is a propyl ester group (-COOCH2CH2CH3). At the 5 position, there is a methyl ester group (-COOCH3).</p>	3784	371.39	103.55	2.91	-4.31
Ibuprofen	 <p>The chemical structure of Ibuprofen is a propionic acid derivative. It consists of a central benzene ring. At the 1 position, there is a propionic acid group (-CH2-CH2-COOH). At the 4 position, there is an isobutyl group (-CH2-CH2-CH(CH3)2).</p>	3672	206.29	37.30	3.61	-3.64

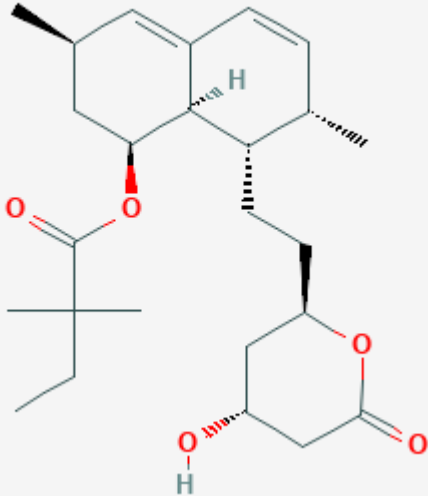
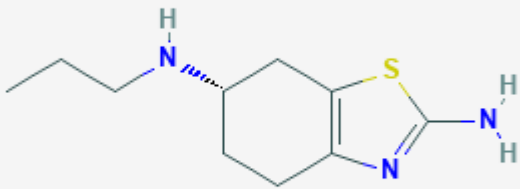
Imatinib	 <p>The image shows the chemical structure of Imatinib, a tyrosine kinase inhibitor. It features a central imidazole ring substituted with a 4-pyridyl group, a 4-methylphenyl group, and a 4-(4-methylpiperidin-1-ylmethyl)benzamide group.</p>	5291	493.62	86.28	2.83	-5.70
Quinacrine Hydrochloride	<p>Cl - H</p>  <p>The image shows the chemical structure of Quinacrine Hydrochloride. It consists of a quinacrine core (a tricyclic system of two benzene rings fused to a central pyrimidine ring) substituted with a chlorine atom at the 8-position, a methyl group at the 6-position, and a diethylaminoethyl side chain at the 4-position. The structure is shown as a hydrochloride salt, with a separate Cl-H label.</p>	6239	399.97	37.39	5.71	-5.68

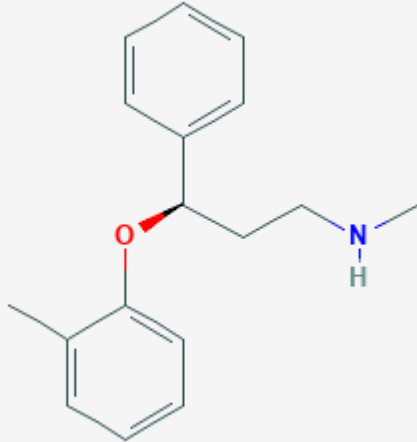
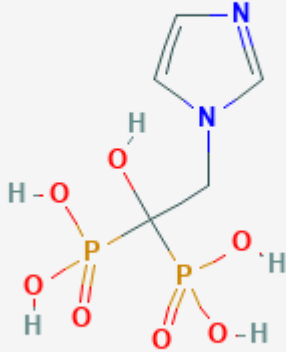
Pyronaridine tetraphosphate		156867	518.06	73.75	6.01	-5.73
Dantrolene		6914273	314.26	120.73	1.86	-4.98

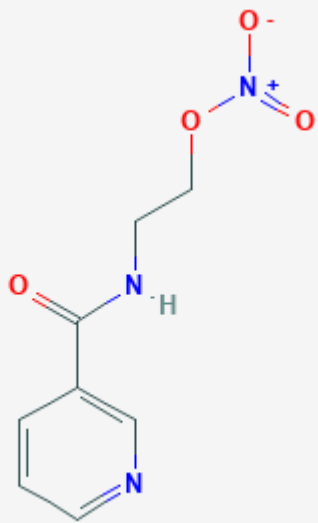
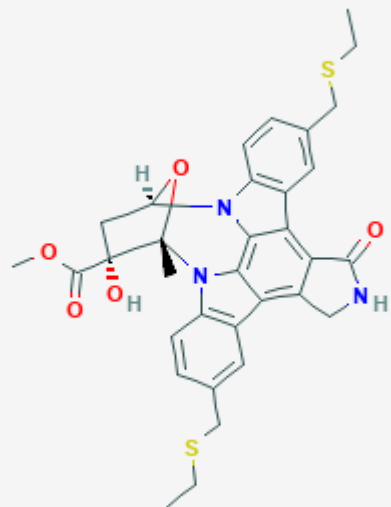
Disulfiram with copper		3117	296.55	70.66	3.32	-6.18
Carvedilol		2585	406.48	75.74	3.97	-5.03

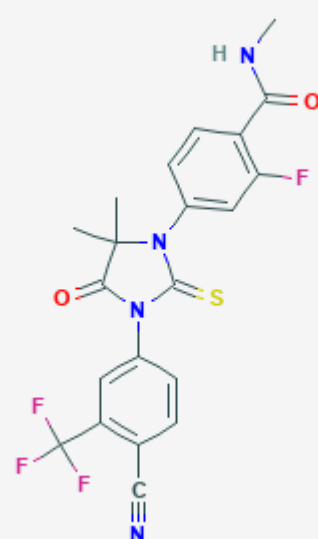
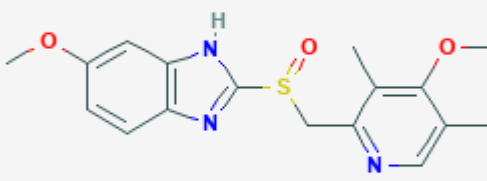
Dexmedetomidine	 <p>The chemical structure of Dexmedetomidine consists of a benzene ring with methyl groups at the 2 and 6 positions. A chiral center is attached to the benzene ring at the 4-position, with a wedged bond to the ring and a dashed bond to a hydrogen atom. This chiral center is also bonded to a hydrogen atom and a 2,5-dihydroimidazole ring.</p>	5311068	200.29	28.68	2.61	-3.09
Prazosin	 <p>The chemical structure of Prazosin features a central imidazole ring. At the 2-position of the imidazole, there is a piperazine ring. At the 4-position of the imidazole, there is a benzene ring with methoxy groups at the 3 and 5 positions. At the 5-position of the imidazole, there is a hydrogen atom. The nitrogen at the 1-position of the piperazine ring is bonded to a carbonyl group, which is further attached to a furan ring.</p>	4893	383.41	106.95	0.19	-4.53

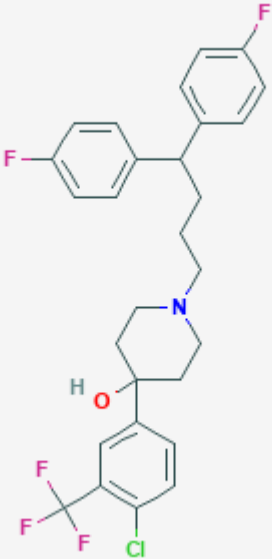
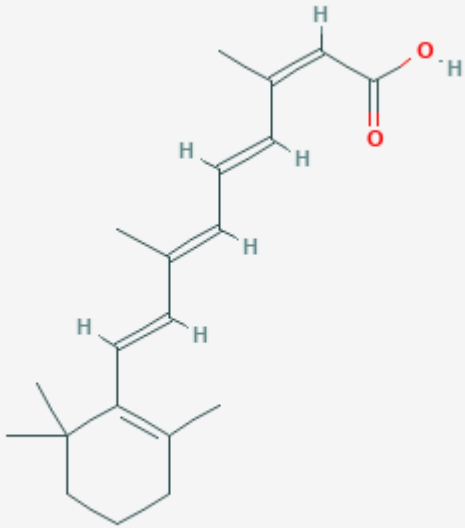
Famotidine	 <p>The chemical structure of Famotidine is shown. It consists of a central 1,2,4-thiazole ring. One nitrogen atom of this ring is substituted with a 2-thioethylamino group (-NH-CH2-CH2-S-). The other nitrogen atom of the thiazole ring is substituted with a 2-mercaptoethylsulfonamide group (-CH2-CH2-S-NH-SO2-NH2).</p>	5702160	337.45	175.83	-0.85	-2.89
Alpha-lipoic acid	 <p>The chemical structure of Alpha-lipoic acid is shown. It features a central 1,2-dithiolane ring (a five-membered ring with two sulfur atoms). A propyl chain is attached to one of the carbon atoms of this ring, ending in a carboxylic acid group (-COOH).</p>	864	206.33	37.30	2.93	-2.52

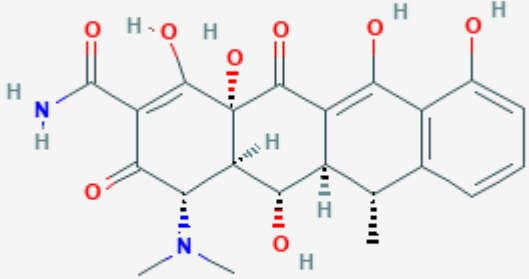
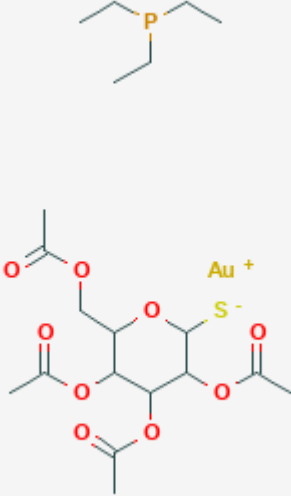
Simvastatin	 <p>The image shows the chemical structure of Simvastatin. It consists of a bicyclic core (a decalin system) with a methyl group on the left ring and a hydrogen atom on the right ring. Attached to the left ring is a side chain containing a hydroxyl group and a carbonyl group. The right ring is connected via a propyl chain to another bicyclic system, which is further substituted with a hydroxyl group and a carbonyl group.</p>	54454	418.57	72.83	4.42	-4.43
Pramipexole	 <p>The image shows the chemical structure of Pramipexole. It features a central benzene ring fused to a five-membered ring containing a sulfur atom and a nitrogen atom. A propylamino group is attached to the benzene ring, and a primary amine group is attached to the five-membered ring.</p>	119570	211.33	50.94	1.35	-1.60

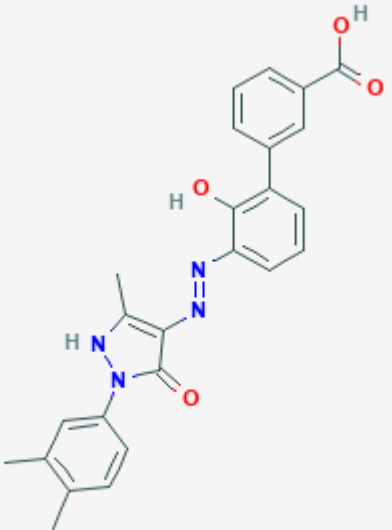
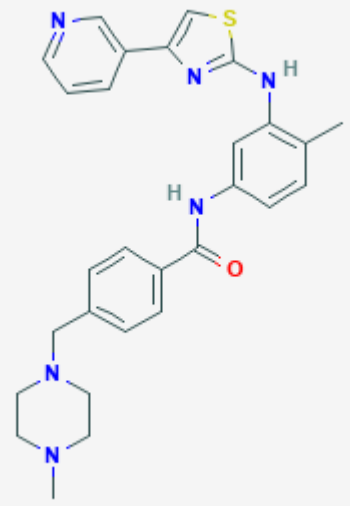
Atomoxetine		54841	255.36	21.26	4.12	-3.33
Zoledronic Acid		68740	272.09	153.11	-3.65	1.55

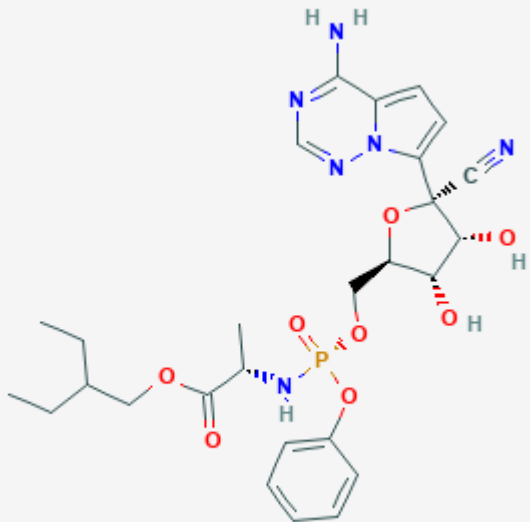
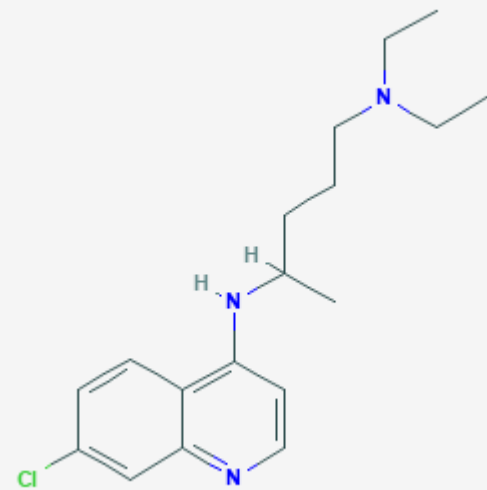
Nicorandil		47528	211.18	97.04	0.01	-1.17
CEP-1347		9917013	615.78	94.72	8.40	-9.41

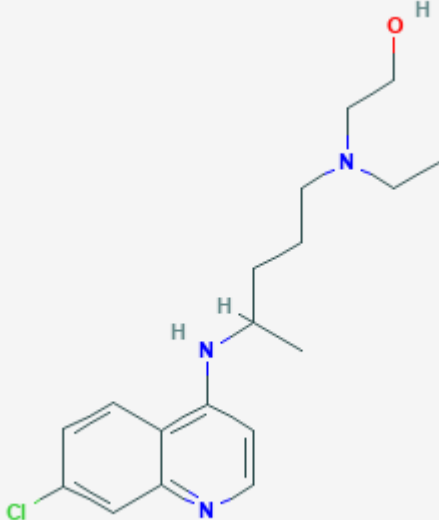
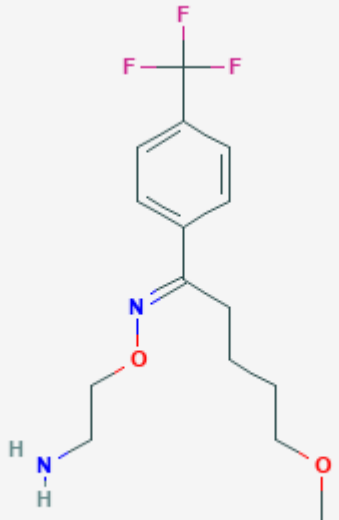
Enzalutamide	 <p>The chemical structure of Enzalutamide is a complex molecule. It features a central imidazole ring system. One nitrogen of the imidazole is substituted with a tert-butyl group and a 2-fluorophenyl group. The other nitrogen is substituted with a 4-(trifluoromethyl)phenyl group and a cyano group. The 2-fluorophenyl group is further substituted with an acetamide group (-NHCH3).</p>	15951529	464.44	108.53	3.78	-7.55
Omeprazole	 <p>The chemical structure of Omeprazole is a benzimidazole derivative. It consists of a benzimidazole ring system where the 5-position is substituted with a methoxy group (-OCH3). The 2-position of the benzimidazole is substituted with a methylene group (-CH2-), which is further substituted with a sulfonyl group (-SO2-). The sulfonyl group is connected to a pyridine ring, which has a methoxy group (-OCH3) at the 3-position and a methyl group (-CH3) at the 4-position.</p>	4594	345.42	96.31	1.32	-3.78

Penfluridol	 <p>The chemical structure of Penfluridol consists of a central piperidine ring. Attached to the piperidine ring are a hydroxyl group (-OH) and a 2-chloro-4-(trifluoromethyl)phenyl group. A propyl chain extends from the nitrogen atom of the piperidine ring, terminating in a 1,1'-bis(4-fluorophenyl)ethane moiety.</p>	33630	523.97	23.47	8.25	-8.18
Isotretinoin	 <p>The chemical structure of Isotretinoin features a cyclohexene ring with two methyl groups at the 1 and 4 positions. A side chain is attached to the ring, consisting of three conjugated double bonds and a terminal carboxylic acid group (-COOH).</p>	5282379	300.44	37.30	4.63	-7.60

Doxycycline	 <p>The image shows the chemical structure of Doxycycline, a tetracycline antibiotic. It features a central tetracycline core with a dimethylamino group at the 7-position and a hydroxyl group at the 4-position. The structure is shown with stereochemistry: the dimethylamino group is dashed, the hydroxyl group is wedged, and the hydroxyl group at the 12-position is dashed.</p>	54671203	444.44	181.62	-0.83	-2.64
Auranofin	 <p>The image shows the chemical structure of Auranofin, a gold(I) complex. It consists of a central gold atom (Au⁺) coordinated to a sulfur atom (S⁻) and three acetate groups. The sulfur atom is part of a cyclic structure that includes a phosphorus atom (P) coordinated to three ethyl groups. The structure is shown with stereochemistry: the gold atom is yellow, the sulfur atom is green, and the phosphorus atom is orange.</p>	24199313	363.36	114.43	0.07	-2.55

Eltrombopag	 <p>The chemical structure of Eltrombopag is a complex molecule. It features a central 5-membered imidazole ring. One nitrogen atom of the imidazole ring is substituted with a 3,4-dimethylphenyl group. The other nitrogen atom is part of a carbonyl group (C=O) and is also bonded to a hydrogen atom. The 2-position of the imidazole ring is connected via a diazo group (-N=N-) to a 3-hydroxyphenyl ring. The 4-position of the imidazole ring is connected to a 4-(4-formylphenyl)phenyl group, which consists of a central phenyl ring attached to another phenyl ring that has a formyl group (-CHO) at the para position.</p>	135449332	442.48	114.59	5.78	-6.82
Masitinib	 <p>The chemical structure of Masitinib is a complex molecule. It features a central 5-membered thiazole ring. One nitrogen atom of the thiazole ring is substituted with a pyridine ring. The other nitrogen atom is part of an NH group and is also bonded to a hydrogen atom. The 2-position of the thiazole ring is connected to a 3-methylphenyl ring. The 4-position of the thiazole ring is connected to a 4-(4-(1-methylpiperazine)methyl)phenyl)phenyl group, which consists of a central phenyl ring attached to another phenyl ring that has a methyl group at the meta position and a 4-(1-methylpiperazine)methyl group at the para position.</p>	10074640	498.65	73.39	3.82	-5.66

Remdesivir	 <p>The image shows the chemical structure of Remdesivir. It features a central ribose sugar ring with a cyano group (-C≡N) at the C2 position and a phosphate group at the C3 position. The phosphate group is linked to a nitrogen atom, which is further connected to a benzyl group and a propanoic acid derivative. The propanoic acid derivative is linked to a 2-aminopyrimidin-5-yl group.</p>	121304016	602.58	203.01	1.75	-5.17
Chloroquine	 <p>The image shows the chemical structure of Chloroquine. It consists of a 4-chloroquinoline ring system. At the 7-position of the quinoline ring, there is a secondary amine group (-NH-) attached to a 4-diethylaminobutyl chain.</p>	2719	319.88	28.16	4.28	-3.78

Hydroxychloroquine		3652	335.88	48.39	3.25	-3.26
Fluvoxamine		5324346	318.34	56.84	3.23	-3.09