Supporting Information

Discovery of Novel and Cardioselective Diltiazem-like Calcium Channel Blockers via Virtual Screening

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Table S1. Table summarizing the threshold values used for the **pharmacokinetic filter** (PK-filter).

Property	Lower Threshold Value	Upper Threshold Value	Description
MW	200	500	The lower MW threshold was set to 200 in order to eliminate trivial and too small compounds, the upper to 500 in order to retain drug-like compounds.
Log P	1	5	The LogP range was set large enough to include compounds that are either mostly hydrophilic or mostly hydrophobic.
Soly	-4	Not Set	Soly is the solubility reported in logarithmic scale: compounds are predicted to have at least a solubility of 100 μM.
Absorption	0.2	Not Set	The absorption-model is based on Caco2 cells data: the minimum value of 0.2 guarantees only absorbable compounds to be considered.
BBB	Not Set	0	BBB is the Blood-Brain Barrier: only compounds which do not penetrate the brain barrier were selected.
Metabolic Stability	0.3	Not Set	Metabolic Stability is referred to the cytochrome P450 3A4, the major responsible for drug metabolism in humans: only compounds with acceptable metabolic stability versus CYP3A4 are retained.

Table S2. Statistics concerning compounds passing the filters. Four databases were used and Sigma-Aldrich was selected because of its higher percentage of N-containing compounds (e).

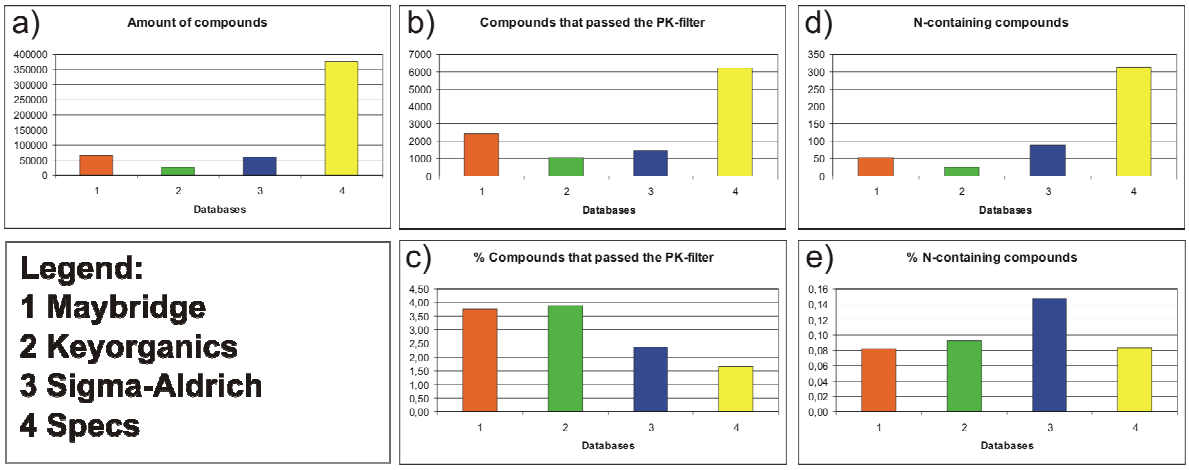

Table S3. ZINC codes, Sigma-Aldrich codes, and IUPAC names for the selected compounds.

Comp	ZINC codes	Sigma-Aldrich Codes	IUPAC names
4	ZINC00406195	R415227	*N*-[2-(Dimethylamino)ethyl]-3-hydroxy-2-naphthamide
5	ZINC00390273	R908940	1-{3-[(Dimethylamino)methyl]-2,4-dihydroxyphenyl}-2-(2-methylphenyl)ethanone
6	ZINC00394865	S469963	*N*-(4-Ethoxyphenyl)-N^3,N^3-diethyl-β-alaninamide
7	ZINC00218019	R407348	*N*,*N*-Dimethyl-*N*'-(2-pyridin-3-ylquinolin-4-yl)ethane-1,2-diamine
8	ZINC00002043	C8278	2-[(4-Chlorophenyl)(pyridin-2-yl)methoxy]-*N*,*N*-dimethylethanamine (Carbinoxamine)
9	ZINC00402771	C1172	1-[(5-Chloro-1-naphthyl)sulfonyl]-1,4-diazepane
10	ZINC00399656	S794740	*N*-(5-Chloro-2-methoxyphenyl)-4-methylpiperazine-1-carboxamide
11	ZINC00389071	R732796	1-[(2-Chlorophenoxy)acetyl]piperazine
12	ZINC00392512	S219061	(1-Methylpiperidin-2-yl)methyl (2-methoxyphenyl)carbamate
13	ZINC00389136	R735884	7-[2-(Diethylamino)ethoxy]-2*H*-chromen-2-one
14	ZINC00032957	R608068	8-[(4-Methylpiperazin-1-yl)sulfonyl]quinoline
15	ZINC00357005	S239534	*N*-(4-*tert*-butyl-2,6-dimethylphenyl)-2-morpholin-4-ylacetamide
16	ZINC00056556	82065	(2*R*)-1-(Isopropylamino)-3-(1-naphthyloxy)propan-2-ol (*R*-(+)-Propranolol)
17	ZINC00395798	L129984	(2*S*)-1-(2-Ethyl-3,5-dimethylphenoxy)-3-(isopropylamino)propan-2-ol
18	ZINC00391049	S46001	*N*-(2-Methyl-2-morpholin-4-ylpropyl)-*N*'-phenylthiourea
19	ZINC00002002	S347108	*N*-(4-Methoxybenzyl)-*N*',*N*'-dimethyl-*N*-pyridin-2-ylethane-1,2-diamine *N*-[(4-Methoxyphenyl)methyl]-*N*',*N*'-dimethyl-*N*-2-pyridinyl-1,2-ethanediamine (Pyrilamine or Mepyramine)
20	ZINC00399019	S761397	(3a*R*,10b*R*,12a*S*)-8,9-Dimethoxy-2,3,3a,5,6,10b,11,12a-octahydrocyclopenta[5,6]pyrido[2,1-*a*]isoquinolin-12(1*H*)-one
21	ZINC00406765	R468967	4-{[Benzyl(methyl)amino]methyl}-2-bromopyridin-3-ol

Table S4. Superposition proposed by SHOP, on the basis of Molecular Interaction Fields, for the selected compounds over the templates **1** and **3**. Nitrogen atoms are represented in blue, oxygen atoms in red, sulphur atoms in orange; carbon atoms are differently coloured (**1** = green, **3** = pink, **4-21** = cyan). Hydrogen atoms are not presented for clarity, whereas the white atom bonded to the nitrogen is the anchor used by SHOP.

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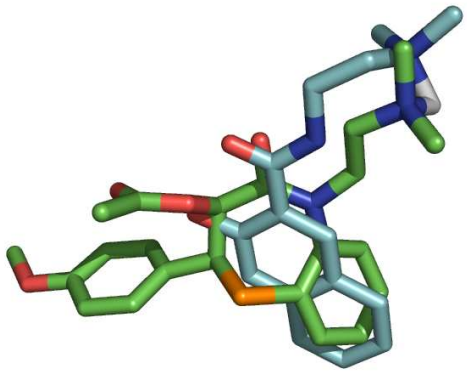
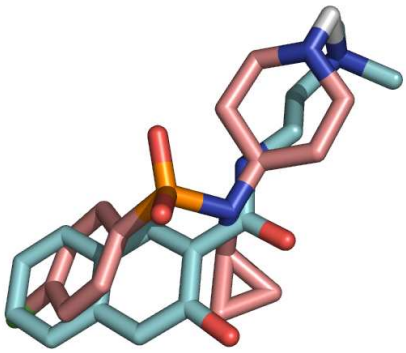
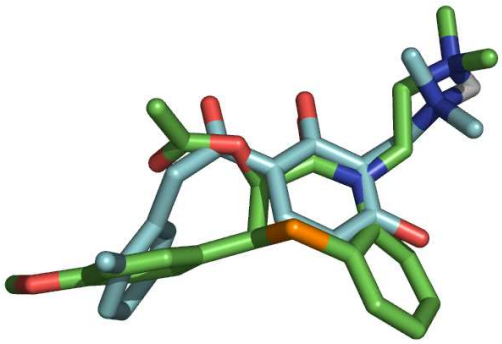
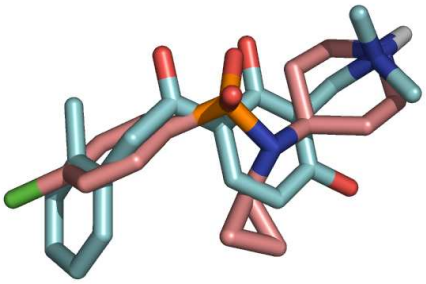
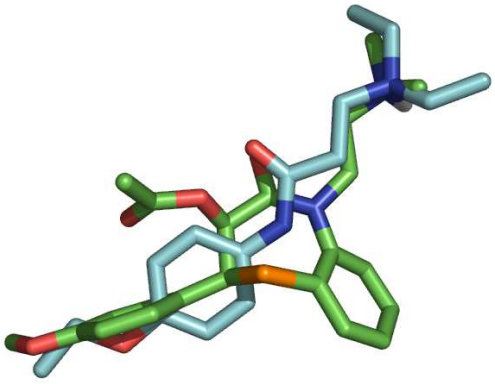
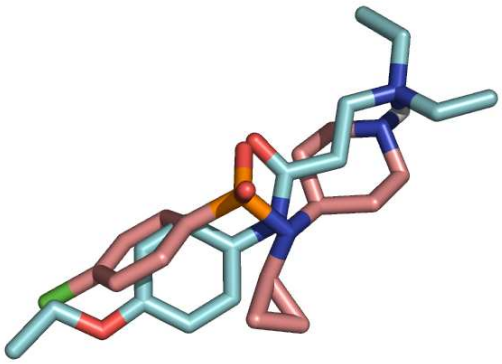
4		
5		
6		

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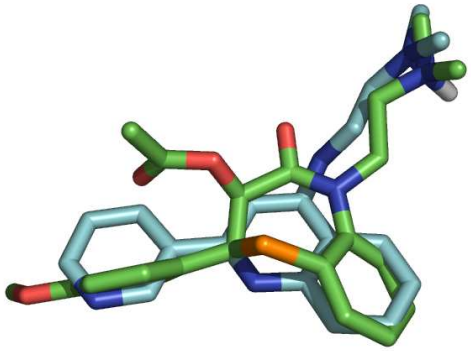
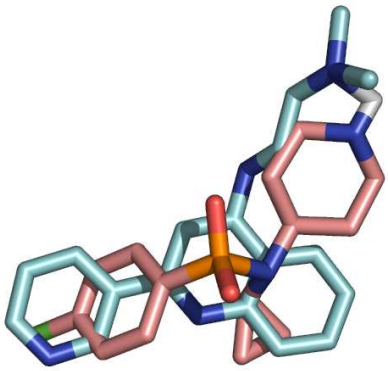
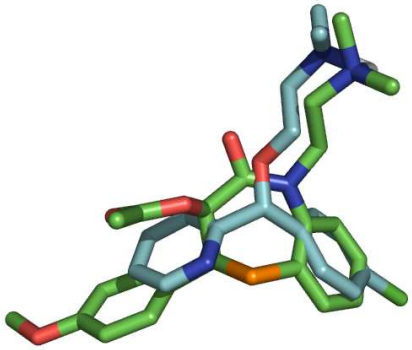
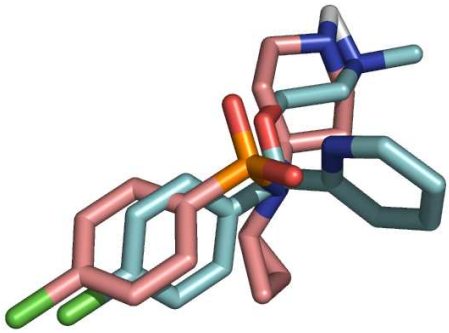
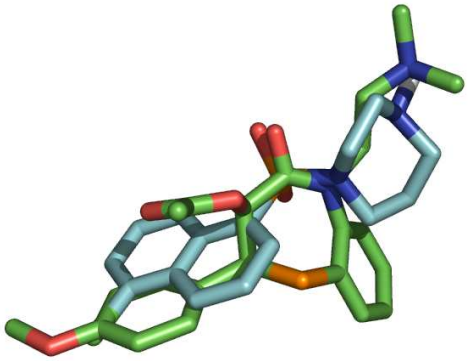
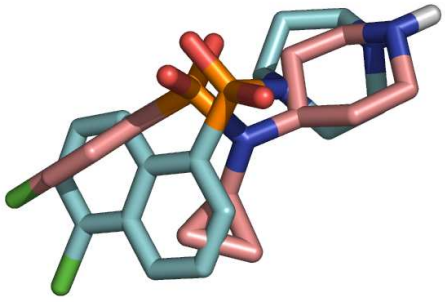
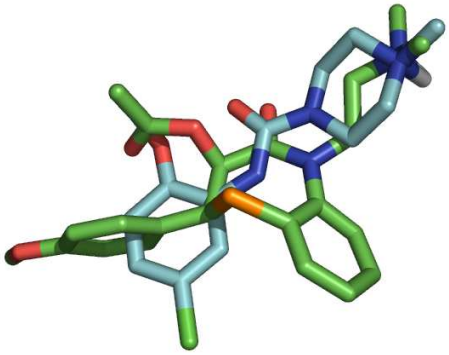
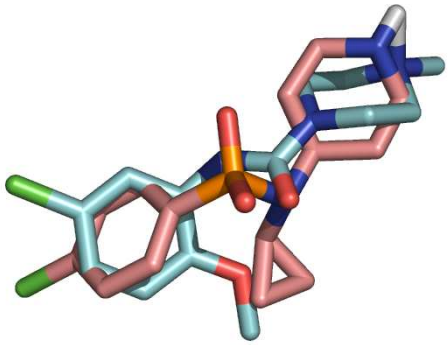
7		
8		
9		
10		

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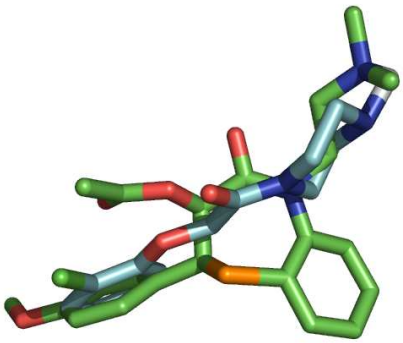
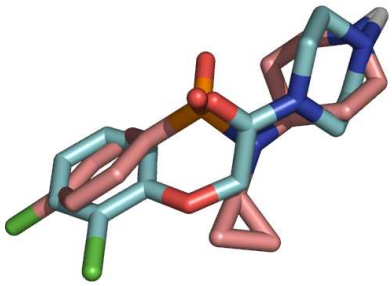
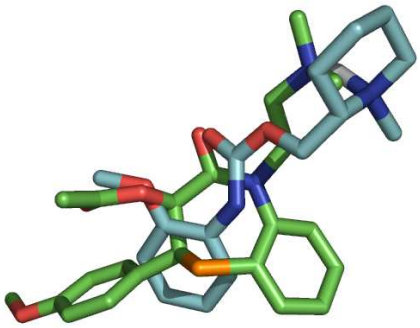
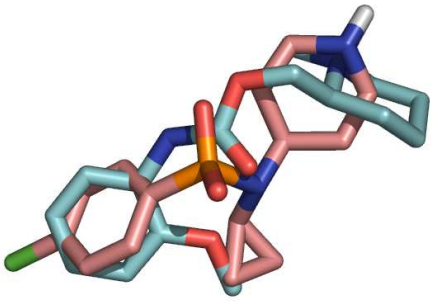
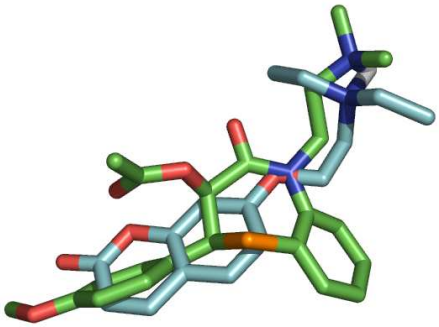
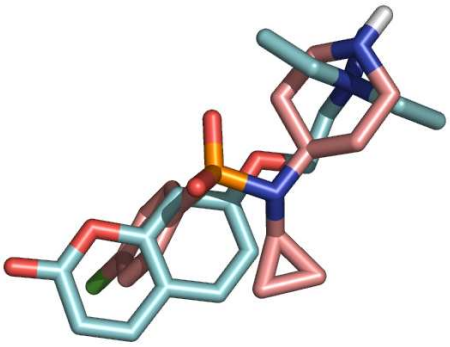
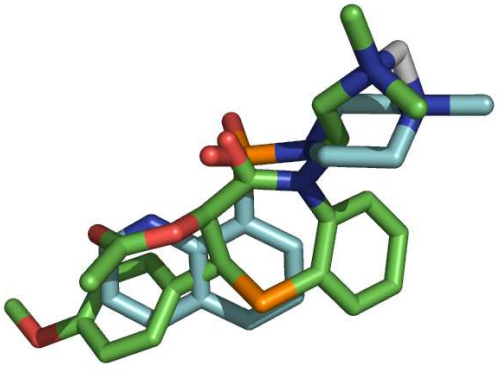
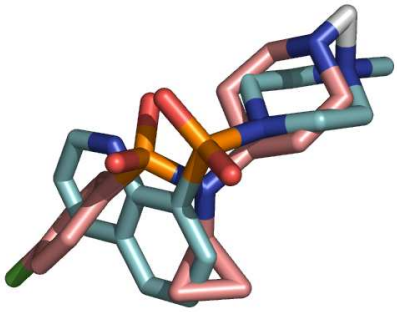
11		
12		
13		
14		

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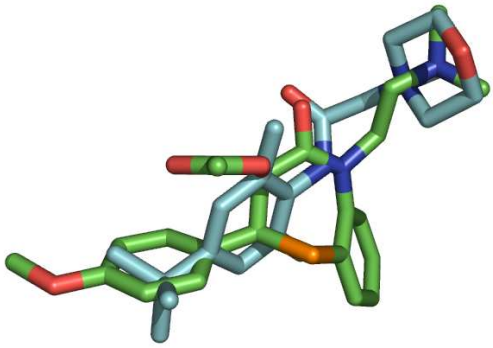
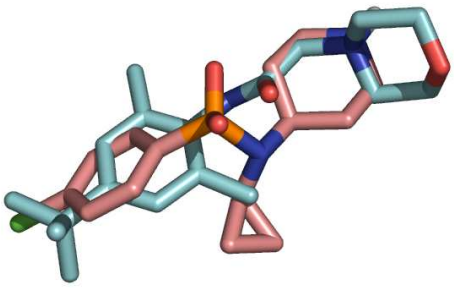
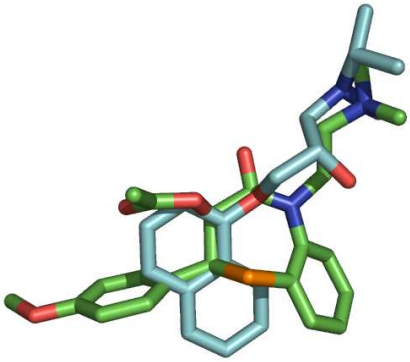
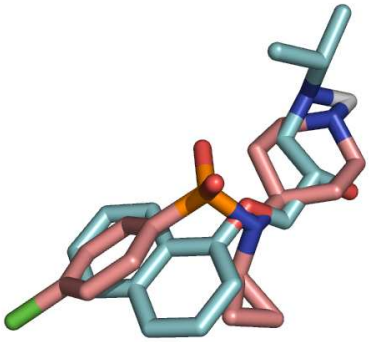
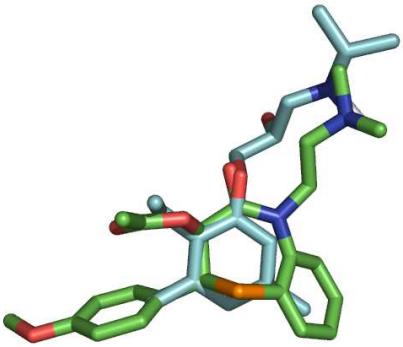
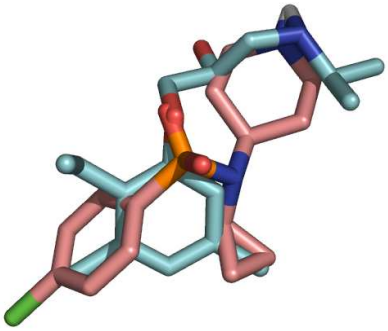
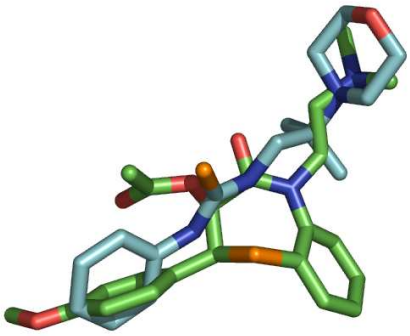
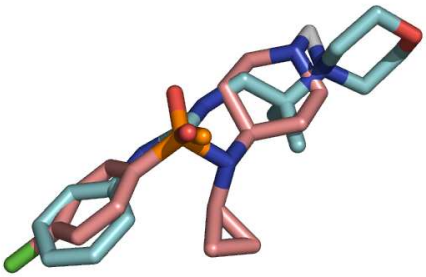
15		
16		
17		
18		

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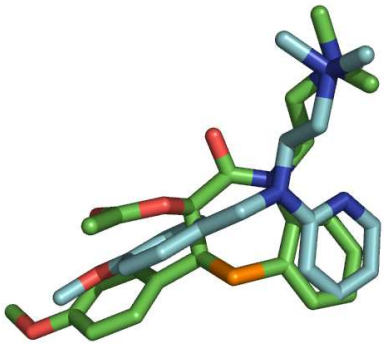
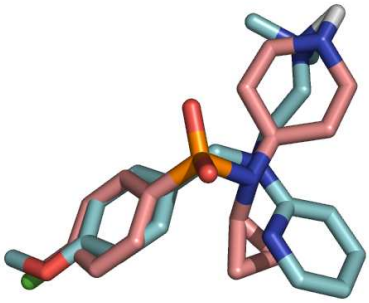
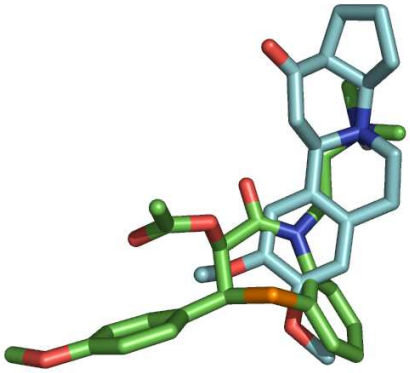
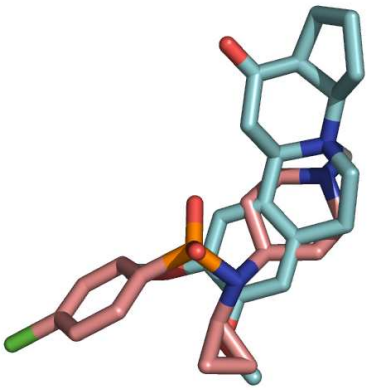
19		
20		
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