

Supporting Information

Synthesis, in vitro activity, and three-dimensional quantitative structure-activity relationship of novel hydrazine inhibitors of human Vascular Adhesion Protein-1

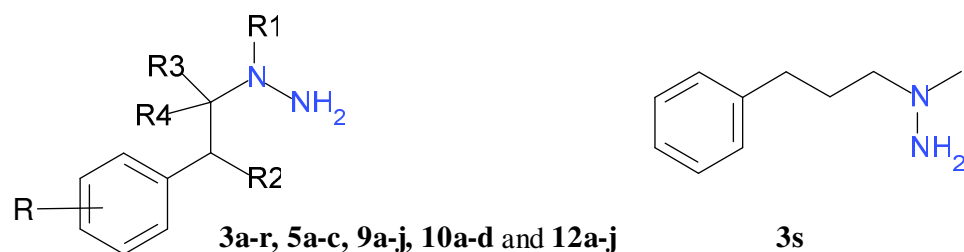
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Supporting Figure 1

Table S1. The melting points of synthesized hydrazine molecules and the number of the submodel where a compound belongs in QSAR model building (see Figure 2).



Compound	Mp (°C)	Set	Compound	Mp (°C)	Set
Phenelzine		1	9a	63-66 ^b	1
3a	93-94 ^a	3	9b	127-128 ^c	3
3b	138-140 ^a	1	9c	86-88 (base)	2
3c	82-84 ^b	4	9d	88-90 ^c	4
3d	97-99 ^a	2	9e	129-131 ^c	3
3e	73-76 ^a	1	9f	103-104 ^b	1
3f	96-98 ^a	3	9g	139-141 ^c	2
3g	61-63 ^b	2	9h	123-127 ^b	4
3h	88-90 ^b	2	9i	143-145 ^b	2
3i	113-115 ^b	2	9j	90-92 ^c	3
3j	84-87 ^b	4	10a ^d	145-146 ^a	1
3k	127-130 ^a	3	10b ^d	141-143 ^b	2
3l	129-131 ^a	4	10c ^d	132-134 ^b	1
3m	76-78 ^b	3	10d	184-186 ^b	2
3n	75-77 ^b	3	12a	108-110 ^c	4
3o	132-134 ^a	4	12b	117-119 ^c	3
3p	189-192 ^a	1	12c	116-118 ^c	2
3q	96-97 ^b	1	12d	98-100 ^b	1
3r	109-111 ^b	2	12e	116-119 ^c	4
3s	71-72 ^b	4	12g	104-107 ^c	4
5a	120-125 ^b	1	12h	122-124 ^c	4
5b	130-133 ^b	4	12i	147-149 ^c	1
5c	117-120 ^b	3	12j	119-120 ^b	3

^aHydrochloride; ^bHydrogen maleate; ^cHydrogen fumarate; ^dRelative configuration 1*R**,2*S**; 1*R**,2*S**; 1*R**,2*S**

Table S2. Statistics of different COMSIA 3D QSAR models.

Model	Data	q^2_{LOO}	r^2	SEE ^a	No. of components	Contribution steric ^b	Contribution electrostatic ^c	Outliers ^d
Steric*	VAP-1	0.636	0.828	0.163	4			0
Hydrophobic*	MAO	0.749	0.840	0.209	3			0
Hydrophobic	VAP-1	0.531	0.769	0.190	4			0
Steric	MAO	0.535	0.769	0.305	3			0
Steric and electrostatic	VAP-1	0.544	0.912	0.110	6	0.614	0.386	1
Steric and electrostatic	MAO	0.634	0.901	0.179	3	0.474	0.526	1

^a Standard error of estimate; ^b Contribution of steric descriptor in models containing both steric and electrostatic features; ^c Contribution of electrostatic descriptor in models containing both steric and electrostatic features; ^d Number of outlier molecules

* The best correlating models, mentioned also in Table 2.

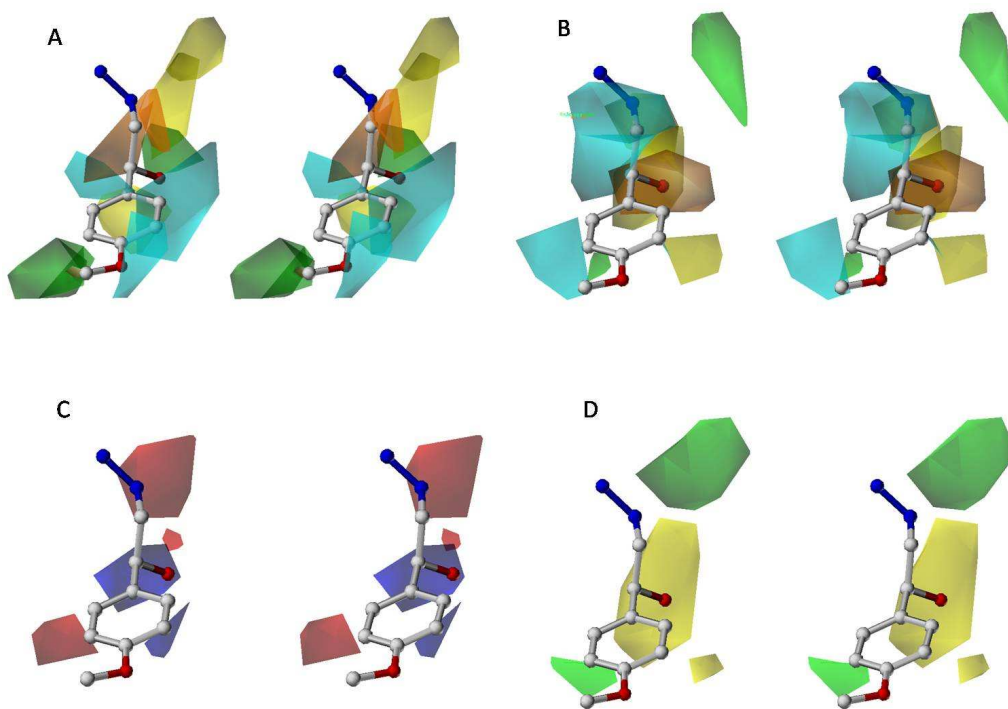


Figure S1. Correlating CoMSIA fields for VAP-1 and MAO. **A** and **B** show the combined steric and electrostatic fields for VAP-1 and MAO, respectively. Green and yellow represent the favorable and disfavorable fields of steric descriptor with contribution levels of 90 % and 25 %, respectively. Orange and cyan represent the favorable regions for electropositive and electronegative fields of electrostatic descriptor with contribution levels of 80 % and 25 %, respectively. **C** represents the hydrophobic CoMSIA field for VAP-1 with favorable blue (80 % contribution) and disfavorable red (25 % contribution). **D** shows the steric CoMSIA fields for MAO with favorable green (90 % contribution) and disfavorable yellow (25 % contribution). The molecule **5c** is shown in ball-and-stick in all panels. All figures are parallel stereo views.