Electronic Supplementary Material (ESI) for RSC Advances.

Investigation of angiotensin-I-converting enzyme (ACE) inhibitory tri-peptides: a combination of 3D-QSAR and molecular docking simulations

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Table S1

Summary of QSAR results for ACE peptides based on template ligand-based alignment.

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R^2_{cv}	0.761	0.667	0.009	0.39	0.449	-0.312	0.824	0.578	0.678
R^2_{ncv}	0.953	0.797	0.466	0.705	0.775	0.166	0.952	0.957	0.67
SEE	0.243	0.479	0.776	0.577	0.549	0.970	0.458	0.248	0.410
F	86.617	37.193	8.276	22.717	11.018	1.884	120.16	55.634	27.649
R^2_{pred}	0.6257	0.4567	0.2113	0.4994	0.428	0.582	0.5199	0.46	0.6783
SEP	0.549	0.613	1.058	0.829	0.859	1.261	0.458	0.776	0.637
N_C	4	2	2	2	5	2	3	6	4
Field contribution									
S	0.675	1.000	-	-	-	-	0.528	0.366	0.439
E	0.325	-	1.000	-	-	-	0.472	-	-
H	-	-	-	1.000	-	-	-	0.634	-
D	-	-	-	-	1.000	-	-	-	0.561
A	-	-	-	-	-	1.000	-	-	-
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R^2_{cv}	0.726	0.532	0.658	0.04	0.426	0.53	0.445	0.625	0.746
R^2_{ncv}	0.941	0.932	0.322	0.659	0.801	0.931	0.916	0.947	0.956
SEE	0.264	0.292	0.322	0.656	0.487	0.287	0.347	0.25	0.237
F	94.216	58.665	31.845	8.206	24.169	80.957	27.139	76.128	91.351
R^2_{pred}	0.459	0.4876	0.7901	0.0241	0.4753	0.4113	0.684	0.5094	0.6199
SEP	0.571	0.768	0.699	1.100	0.827	0.819	0.891	0.687	0.566
N_C	3	4	6	4	3	6	6	4	4
Field contribution									
S	0.618	-	-	-	-	-	-	0.237	0.319
E	-	0.364	0.292	0.653	-	-	-	0.301	0.266
H	-	0.636	-	-	0.567	0.675	-	0.462	-
D	-	-	0.708	-	0.433	-	0.670	-	0.414

A	0.382	-	-	0.347	-	0.325	0.330	-	-
CoMSIA									
	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R^2_{cv}	0.778	0.553	0.649	0.74	0.532	0.558	0.581	0.585	0.613
R^2_{ncv}	0.952	0.850	0.971	0.968	0.947	0.956	0.917	0.967	0.956
SEE	0.240	0.423	0.202	0.214	0.266	0.236	0.343	0.218	0.242
F	117.73	33.883	85.198	75.773	57.387	91.664	27.777	72.333	69.947
R^2_{pred}	0.5015	0.6328	0.6427	0.6615	0.6693	0.6138	0.7827	0.7628	0.6428
SEP	0.514	0.729	0.708	0.609	0.792	0.747	0.774	0.770	0.720
N_C	3	3	6	6	5	4	6	6	5
Field contribution									
S	0.444	0.220	0.249	0.307	-	-	-	-	0.181
E	0.311	-	-	-	0.265	0.215	0.170	-	0.237
H	-	0.404	0.445	-	0.422	0.542	-	0.393	0.304
D	-	0.376	-	0.377	0.322	-	0.623	0.304	0.278
A	0.244	-	0.305	0.315	-	0.242	0.207	0.303	-

CoMSIA					
	SEHA	SEDA	SHDA	EHDA	SEHDA
R^2_{cv}	0.643	0.757	0.664	0.579	0.651
R^2_{ncv}	0.953	0.969	0.970	0.965	0.962
SEE	0.244	0.210	0.205	0.243	0.224
F	85.921	78.174	82.171	69.345	82.040
R^2_{pred}	0.4916	0.6969	0.6684	0.6767	0.6323
SEP	0.671	0.589	0.693	0.751	0.684
N_C	4	6	6	5	5
Field contribution					
S	0.202	0.295	0.175	-	0.157
E	0.191	0.144	-	0.156	0.145
H	0.404	-	0.282	0.362	0.265
D	-	0.354	0.263	0.281	0.246
A	0.204	0.207	0.280	0.200	0.187

Table S2.

Summary of QSAR results for ACE peptides based on docking-based alignment.

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R^2_{cv}	0.005	0.174	-0.162	0.202	-0.197	0.208	-0.057	0.193	0.245
R^2_{ncv}	0.858	0.816	0.812	0.892	0.635	0.892	0.900	0.931	0.983
SEE	0.411	0.468	0.487	0.359	0.642	0.369	0.354	0.296	0.158
F	36.386	26.623	18.334	49.448	16.514	35.165	38.392	56.982	140.992
R^2_{pred}	6E-5	0.1141	0.1596	0.0088	0.019	0.0257	0.0003	0.119	0.1819
SEP	1.089	0.992	1.210	0.975	1.162	0.999	1.155	1.009	1.039

N_C	3	3	4	3	2	4	4	4	6
Field contribution									
S	0.546	1.000	-	-	-	-	0.484	0.376	0.465
E	0.454	-	1.000	-	-	-	0.516	-	-
H	-	-	-	1.000	-	-	-	0.624	-
D	-	-	-	-	1.000	-	-	-	0.535
A	-	-	-	-	-	1.000	-	-	-
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R^2_{cv}	0.288	0.126	-0.104	0.056	0.163	0.268	0.026	0.127	-0.002
R^2_{ncv}	0.981	0.92	0.869	0.793	0.945	0.856	0.928	0.930	0.914
SEE	0.166	0.317	0.407	0.483	0.264	0.403	0.301	0.298	0.329
F	126.43	49.191	28.176	36.67	72.654	56.480	55.018	56.242	45.275
R^2_{pred}	0.0028	0.0608	0.0765	0.0755	0.0001	1E-05	0.0108	0.0038	0.0006
SEP	1.008	1.050	1.180	1.032	1.027	0.909	0.108	1.049	1.124
N_C	6	4	4	2	4	2	4	4	4
Field contribution									
S	0.402	-	-	-	-	-	-	0.253	0.312
E	-	0.404	0.508	0.446	-	-	-	0.298	0.333
H	-	0.596	-	-	0.590	0.507	-	0.449	-
D	-	-	0.492	-	0.410	-	0.393	-	0.355
A	0.598	-	-	0.554	-	0.493	0.607	-	-
CoMSIA									
	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R^2_{cv}	0.096	0.192	0.234	0.176	0.097	0.181	0.02	0.208	0.102
R^2_{ncv}	0.934	0.986	0.948	0.936	0.928	0.836	0.921	0.944	0.939
SEE	0.288	0.141	0.256	0.284	0.300	0.430	0.316	0.265	0.278
F	60.507	177.47	77.748	62.304	55.089	48.428	49.493	72.191	64.890
R^2_{pred}	0.0238	0.0755	0.0092	0.0025	0.0605	0.0017	0.0199	0.0011	0.0007
SEP	1.068	1.075	0.983	1.019	1.067	0.961	1.111	0.999	1.064
N_C	4	6	4	4	4	2	4	4	4
Field contribution									
S	0.274	0.255	0.234	0.292	-	-	-	-	0.200
E	0.292	-	-	-	0.283	0.285	0.302	-	0.221
H	-	0.416	0.388	-	0.428	0.364	-	0.388	0.341
D	-	0.329	-	0.295	0.288	-	0.290	0.255	0.239
A	0.434	-	0.377	0.413	-	0.351	0.408	0.357	-
CoMSIA									

	SEHA	SEDA	SHDA	EHDA	SEHDA
R^2_{cv}	0.159	0.056	0.216	0.164	0.147
R^2_{ncv}	0.941	0.930	0.952	0.936	0.944
SEE	0.273	0.297	0.245	0.284	0.265
F	67.663	56.660	85.170	62.241	72.263

R^2_{pred}	0.0018	0.0096	0.004	0.0259	0.0034
SEP	1.030	1.091	0.994	1.027	1.037
N_C	4	4	4	4	4
Field contribution					
S	0.179	0.217	0.11	-	0.154
E	0.206	0.226	-	0.203	0.166
H	0.317	-	0.308	0.311	0.262
D	-	0.236	0.211	0.203	0.177
A	0.298	0.322	0.289	0.283	0.241

Table S3.

Summary of QSAR results for ACE peptides based on common scaffold-based alignment .

	CoMFA	CoMSIA							
	SE	S	E	H	D	A	SE	SH	SD
R^2_{cv}	-0.133	0.147	-0.213	0.416	-0.234	-0.475	-0.188	0.367	0.066
R^2_{ncv}	0.985	0.862	0.405	0.908	0.951	0.324	0.504	0.931	0.991
SEE	0.140	0.395	0.798	0.323	0.265	0.851	0.729	0.279	0.115
F	215.94	59.186	13.621	93.384	48.510	9.598	20.291	127.84	269.813
R^2_{pred}	0.1154	0.1166	0.1011	0.6411	0.0231	0.1531	0.386	0.4164	0.0009
SEP	1.232	0.981	1.140	0.812	1.328	1.257	1.128	0.845	1.155
N_C	5	2	1	2	6	1	1	2	6
Field contribution									
S	0.675	1.000	-	-	-	-	0.324	0.292	0.337
E	0.325	-	1.000	-	-	-	0.676	-	-
H	-	-	-	1.000	-	-	-	0.708	-
D	-	-	-	-	1.000	-	-	-	0.663
A	-	-	-	-	-	1.000	-	-	-
CoMSIA									
	SA	EH	ED	EA	HD	HA	DA	SEH	SED
R^2_{cv}	-0.337	0.222	-0.268	-0.313	0.338	0.181	-0.387	0.173	-0.193
R^2_{ncv}	0.961	0.994	0.789	0.421	0.996	0.997	0.982	0.988	0.844
SEE	0.229	0.096	0.501	0.788	0.077	0068	0.162	0.128	0.431
F	78.588	387.93	22.458	14.547	593.27	770.31	133.32	259.42	32.398
R^2_{pred}	0.4345	0.3783	0.0562	0.3222	0.3911	0.5325	0.1544	0.246	0.1782
SEP	1.338	1.254	1.229	1.186	0.972	1.082	1.408	1.053	1.192
N_C	5	6	3	1	6	6	6	5	3
Field contribution									
S	0.426	-	-	-	-	-	-	0.206	0.208
E	-	0.351	0.395	0.511	-	-	-	0.275	0.305
H	-	0.649	-	-	0.525	0.629	-	0.520	-
D	-	-	0.605	-	0.475	-	0.602	-	0.487
A	0.57	-	-	0.489	-	0.371	0.398	-	-
CoMSIA									

	SEA	SHD	SHA	SDA	EHD	EHA	EDA	HDA	SEHD
R^2_{cv}	-0.301	0.311	0.13	-0.131	0.238	0.062	-0.32	0.158	0.209
R^2_{ncv}	0.477	0.996	0.986	0.994	0.997	0.995	0.440	0.998	0.997
SEE	0.748	0.072	0.137	0.093	0.067	0.086	0.775	0.058	0.067
F	18.261	682.53	224.72	406.62	788.89	480.87	15.700	1063.9	784.446
R^2_{pred}	0.4822	0.2337	0.4592	0.1004	0.1366	0.4134	0.1946	0.463	0.1005
SEP	1.181	0.992	1080	1.271	1.043	1.158	1.189	1.097	1.063
N_C	1	6	5	6	6	6	1	6	6
Field contribution									
S	0.197	0.169	0.209	0.231	-	-	-	-	0.135
E	0.411	-	-	-	0.197	0.254	0.295	-	0.169
H	-	0.421	0.493	-	0.426	0.468	-	0.411	0.361
D	-	0.409	-	0.466	0.377	-	0.423	0.361	0.335
A	0.392	-	0.298	0.303	-	0.278	0.282	0.228	-

CoMSIA

	SEHA	SEDA	SHDA	EHDA	SEHDA
R^2_{cv}	0.047	-0.234	0.168	0.093	0.096
R^2_{ncv}	0.996	0.994	0.998	0.997	0.997
SEE	0.078	0.090	0.057	0.066	0.064
F	591.463	434.943	1087.702	808.664	881.448
R^2_{pred}	0.2907	0.0478	0.3037	0.2797	0.1973
SEP	1.167	1.328	1.090	1.138	1.137
N_C	6	6	6	6	6
Field contribution					
S	0.156	0.176	0.140	-	0.115
E	0.211	0.199	-	0.171	0.148
H	0.389	-	0.342	0.337	0.293
D	-	0.362	0.320	0.296	0.266
A	0.244	0.263	0.198	0.196	0.178

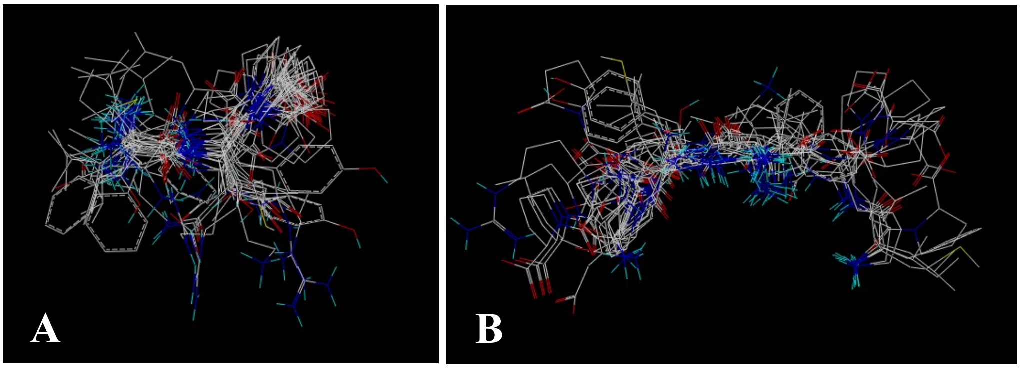

Fig. S1 (A) The alignment for ACE from the docking-based alignment. (B) The alignment for ACE from the common scaffold-based alignment.