Development of coumarin-inspired bifunctional hybrids as a new class of anti-Alzheimer's agents with potent *in vivo* efficacy

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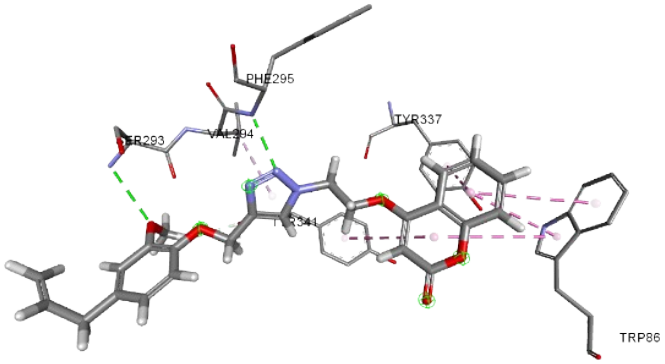
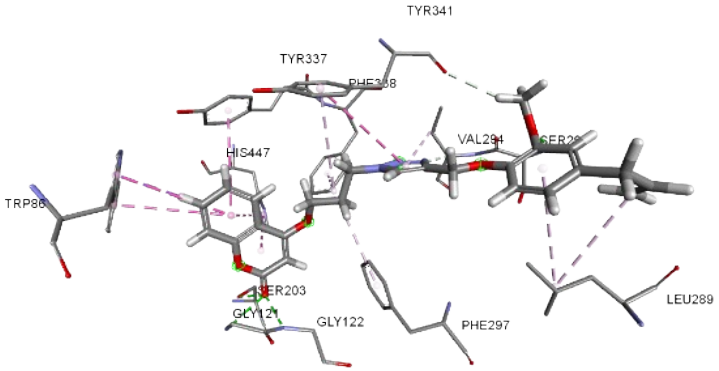
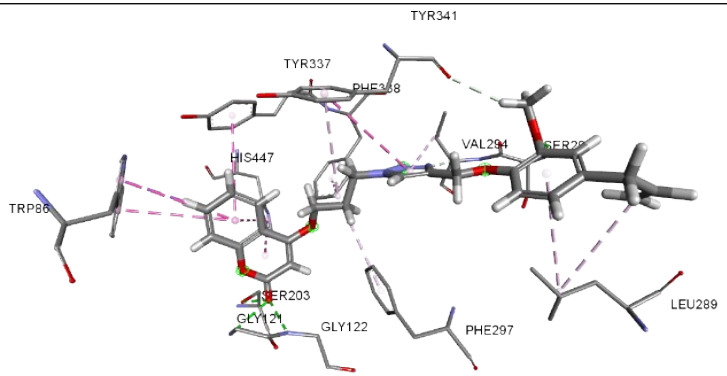
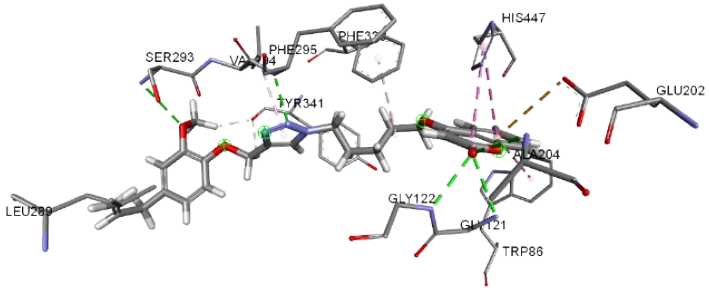
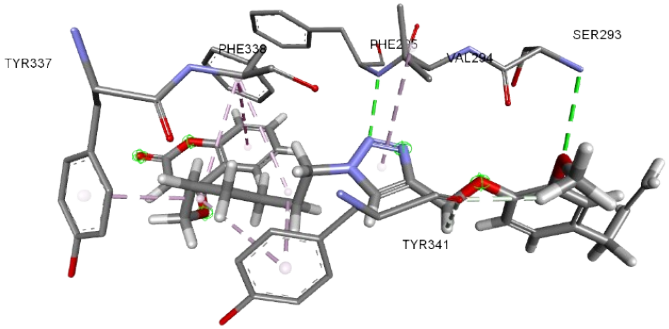
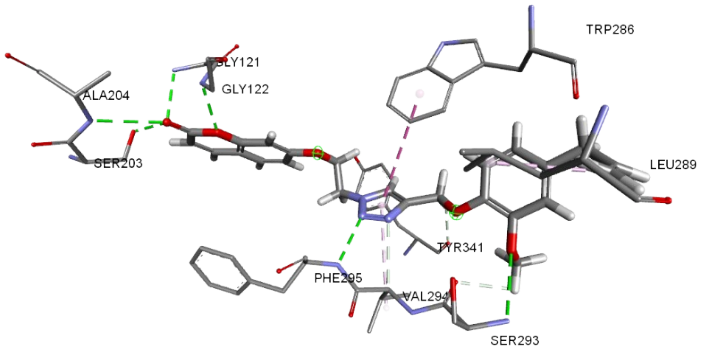
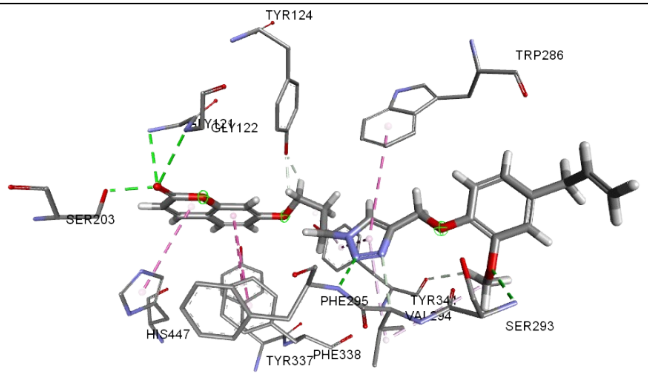
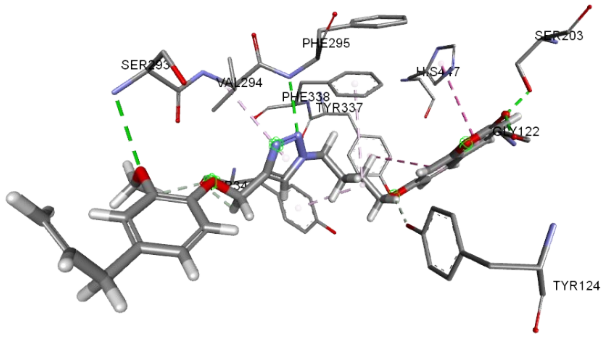
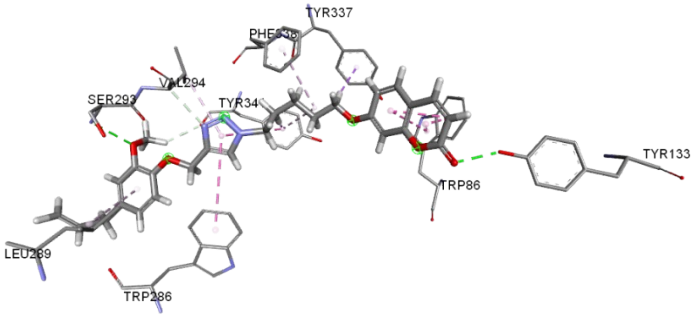
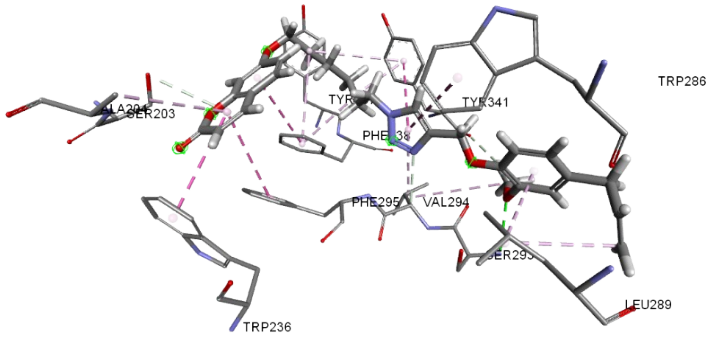
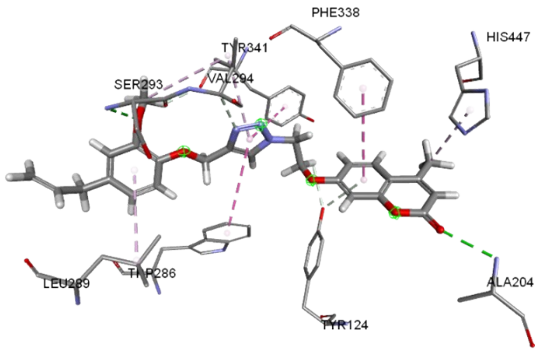
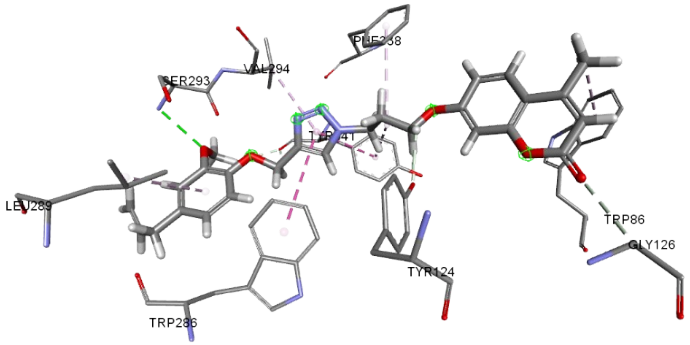
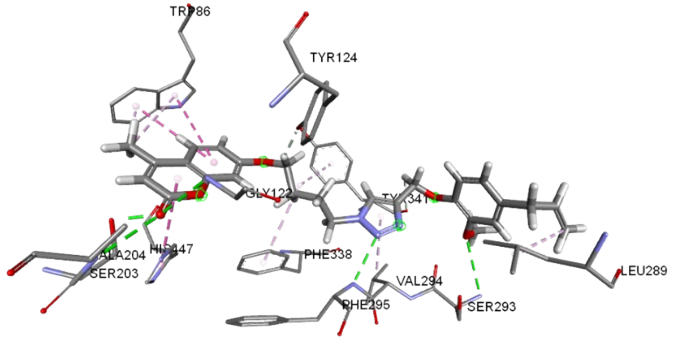
Table 1. Protein-ligand interactions, dock scores, and binding energy (ΔG) of hybrid molecules.

Compound	Ligand Interactions	Dock score	Binding energy (ΔG) Kj/mol
AS1		-25.8367	-12
AS2		-29.8742	-2

AS3		-22.9106	4
AS4		-25.3112	-4

AS5		-23.0363	-33
AS6		-31.3264	-7
AS7		-25.3042	-13

AS8		-28.8645	-13
AS9		-20.9002	-22
AS10		-21.3697	-8

AS11		-26.3132	-7
AS12		-22.0890	-12
AS13		-25.4282	4

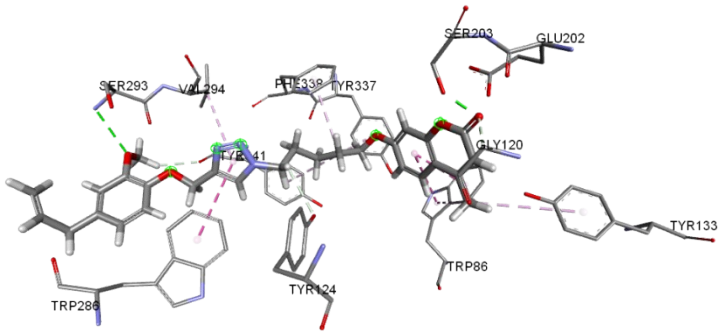
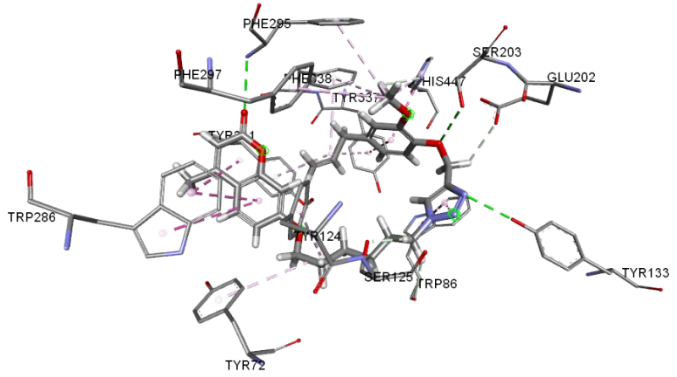
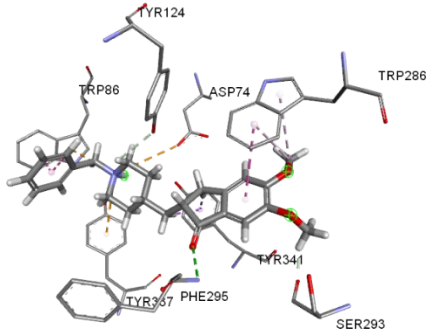
AS14		-21.3793	-22
AS15		-21.6765	-57
Donepezil		-28.7716	-43

Table 2. Lipinski parameters of hybrid molecules.

Compound	mi log *P*	TPSA ((Å^2)	MW (g/mol)	nON	nOHNH
AS1	3.84	88.63	433.46	8	0
AS2	4.11	88.63	447.49	8	0
AS3	4.38	88.63	461.52	8	0
AS4	4.89	88.63	475.55	8	0
AS5	5.39	88.63	489.57	8	0
AS6	3.89	88.63	433.46	8	0
AS7	4.16	88.63	447.49	8	0
AS8	4.43	88.63	461.52	8	0
AS9	4.94	88.63	475.55	8	0
AS10	5.44	88.63	489.57	8	0
AS11	4.27	88.63	447.49	8	0
AS12	4.54	88.63	461.52	8	0
AS13	4.81	88.63	475.55	8	0
AS14	5.31	88.63	489.57	8	0
AS15	5.82	88.63	503.60	8	0

Table 3. ADME properties of hybrid molecules.

Compound	BBB	CYP2D6 substrate	CYP3A4 substrate	HIA	MDCK	PPB
AS1	0.2779	Non	Substrate	98.84	25.7343	90.50
AS2	0.7409	Non	Substrate	98.67	0.2277	92.72
AS3	0.6422	Non	Substrate	98.50	0.7565	90.95
AS4	0.0917	Non	Substrate	98.33	0.3145	91.02
AS5	0.0171	Non	Substrate	98.17	18.8922	91.31
AS6	0.8983	Non	Substrate	98.84	6.3194	91.63
AS7	0.1875	Non	Substrate	98.67	1.8036	93.53
AS8	0.0224	Non	Substrate	98.50	2.7041	91.52
AS9	0.2168	Non	Substrate	98.33	5.2719	91.40
AS10	0.0369	Non	Substrate	98.17	36.2571	91.52
AS11	1.0996	Non	Substrate	98.67	9.7944	91.33
AS12	0.0406	Non	Substrate	98.50	0.6764	93.09
AS13	0.0237	Non	Substrate	98.33	11.1126	91.32
AS14	0.1722	Non	Substrate	98.17	8.3560	91.23
AS15	0.0453	Non	Substrate	98.02	41.4197	91.32