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Identification of effective natural compounds as HIF-1Alpha mimetics for diabetic wound healing; A systematic *in-silico* study

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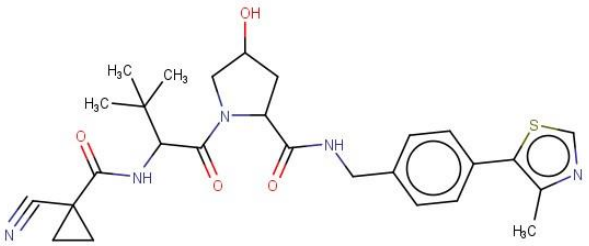
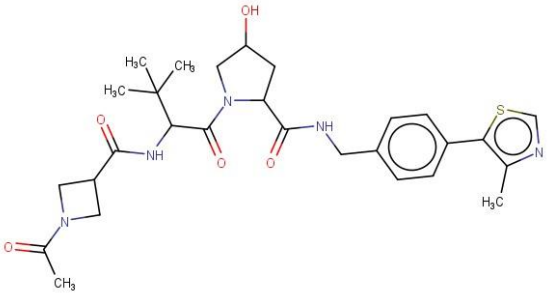
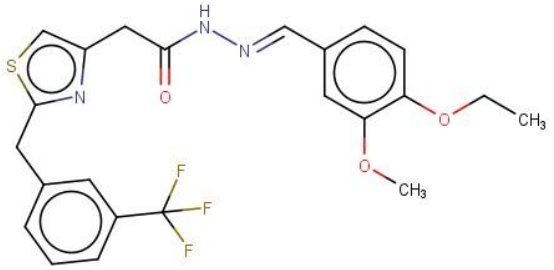
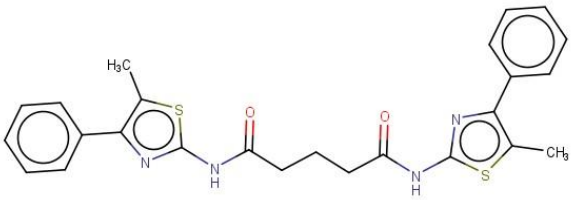
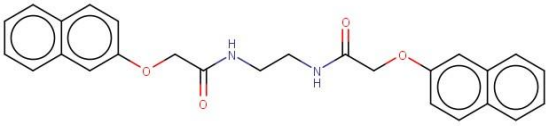
Supplementary Figures:

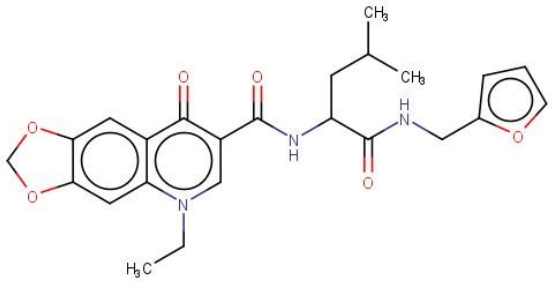
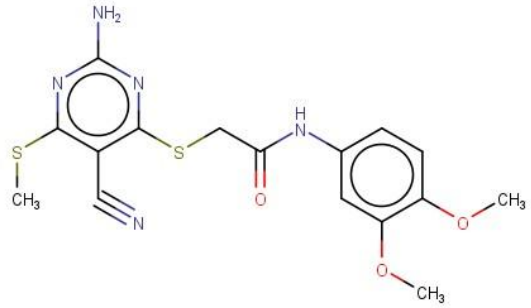
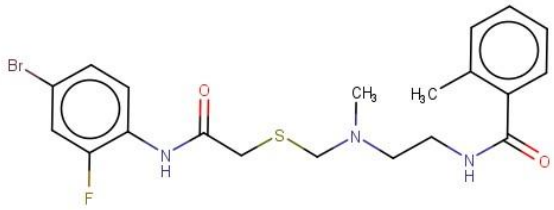
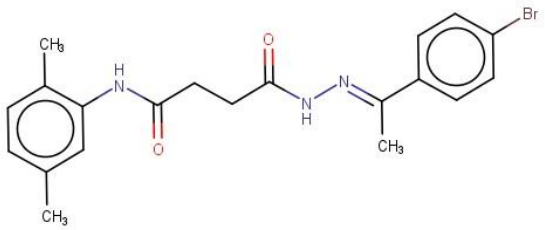
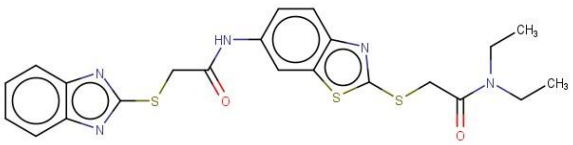
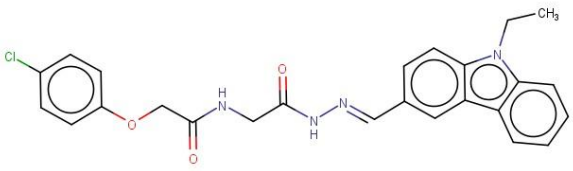
Figure 1. Primary output file of PharmaGist.

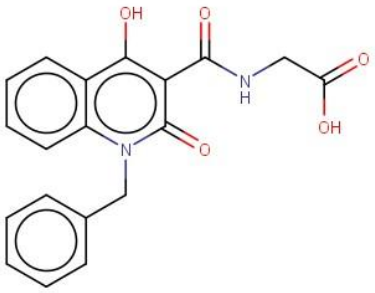
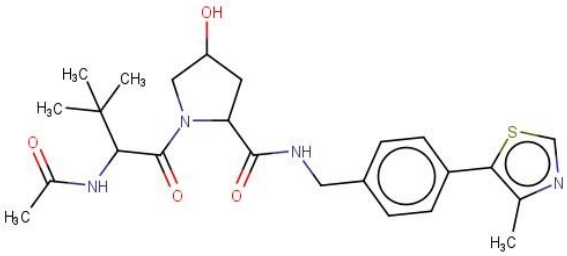
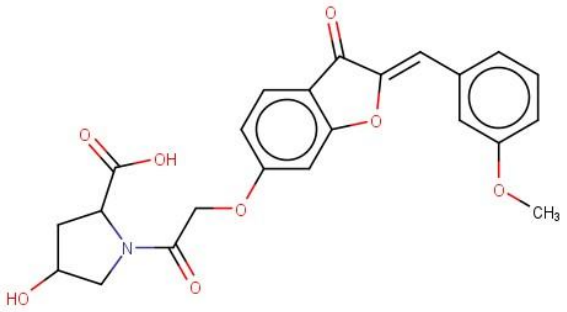
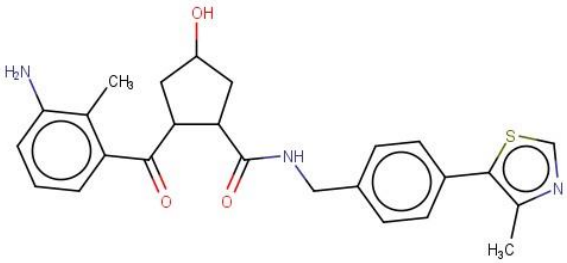
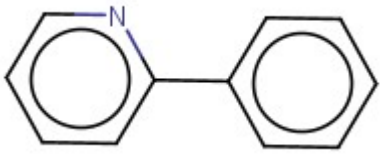
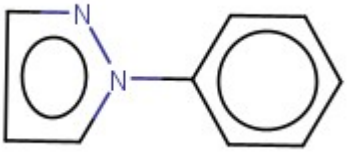
#	Molecule	Atoms	Features	Spatial Features	Aromatic	Hydrophobic	Donors	Acceptors	Negatives	Positives
1	36MOL2.mol2	44	11	11	2	9	0	0	0	0
2	4MOL2.mol2	72	16	13	3	3	4	6	0	0
3	28MOL2.mol2	55	24	22	0	15	3	6	0	0
4	5MOL2.mol2	69	18	16	4	4	4	6	0	0
5	32MOL2.mol2	13	7	5	0	0	2	4	1	0
6	9MOL2.mol2	56	19	15	4	0	5	9	0	1
7	38MOL2.mol2	66	21	18	4	4	8	5	0	0
8	12MOL2.mol2	68	17	15	4	2	6	5	0	0
9	8MOL2.mol2	51	17	15	2	3	4	8	0	0
10	30MOL2.mol2	27	10	9	0	2	1	6	1	0
11	21MOL2.mol2	31	3	3	2	0	1	0	0	0
12	34MOL2.mol2	15	5	5	0	1	0	3	1	0
13	2MOL2.mol2	81	26	21	2	10	8	6	0	0
14	1MOL2.mol2	38	9	9	3	0	1	5	0	0
15	29MOL2.mol2	45	8	7	2	2	2	2	0	0
16	37MOL2.mol2	21	9	8	0	4	1	3	1	0
17	35MOL2.mol2	32	7	6	1	4	1	1	0	0
18	7MOL2.mol2	68	21	18	4	6	5	6	0	0
19	16MOL2.mol2	61	17	14	3	2	3	8	1	0
20	3MOL2.mol2	83	24	19	2	8	8	6	0	0
21	23MOL2.mol2	33	4	4	3	0	1	0	0	0
22	26MOL2.mol2	83	28	24	1	15	7	5	0	0
23	33MOL2.mol2	26	8	7	1	3	1	3	0	0
24	22MOL2.mol2	28	4	3	2	0	1	1	0	0
25	13MOL2.mol2	72	15	12	4	1	5	4	0	1
26	27MOL2.mol2	71	22	18	2	8	6	6	0	0
27	31MOL2.mol2	22	3	3	2	0	1	0	0	0
28	24MOL2.mol2	30	4	4	2	0	2	0	0	0
29	11MOL2.mol2	59	15	13	2	6	5	2	0	0
30	25MOL2.mol2	50	14	12	3	1	3	6	1	0
31	15MOL2.mol2	72	22	18	2	8	7	5	0	0
32	14MOL2.mol2	53	14	11	3	0	4	5	1	1

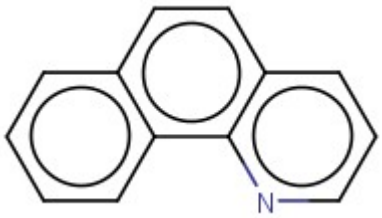
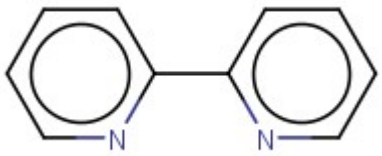
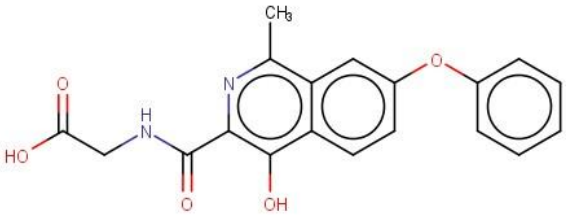
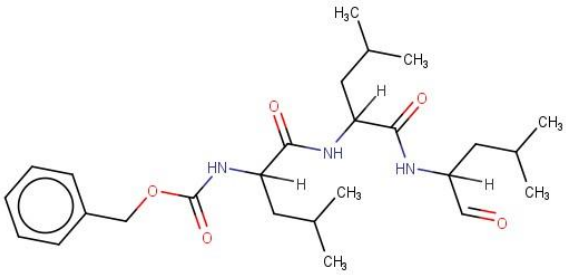
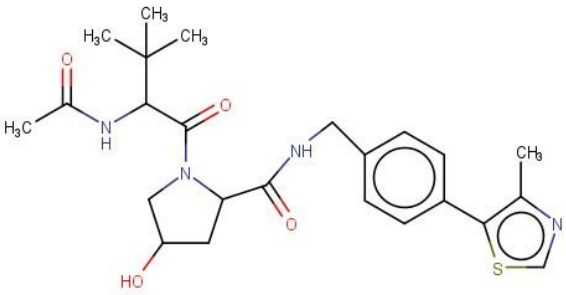
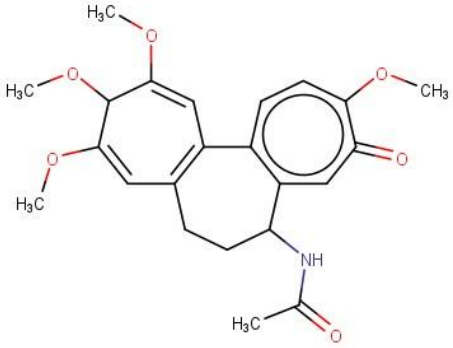
Tables:

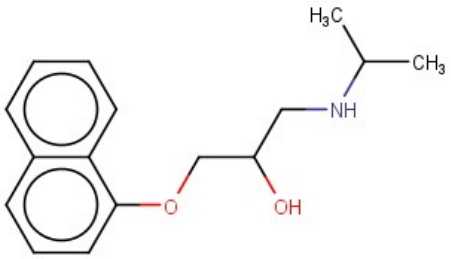
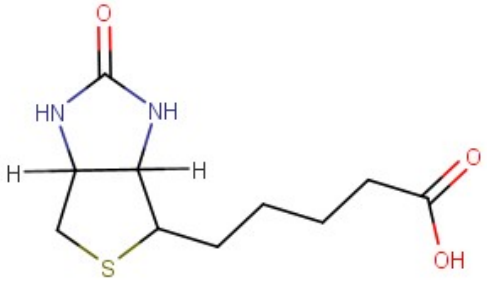
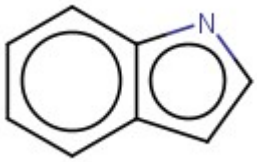
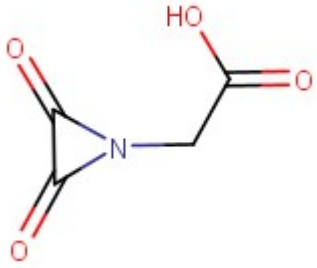
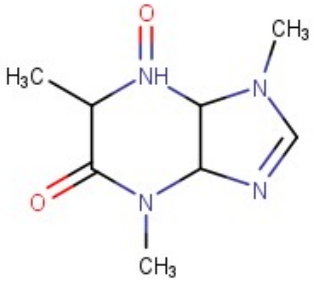
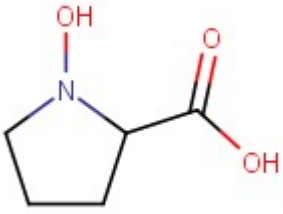
Supplementary Table 1. Data set of input selected for Pharmacophore generation.

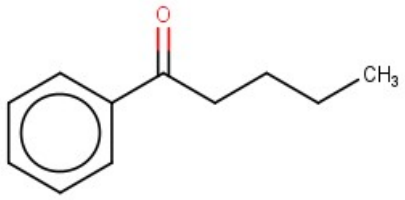
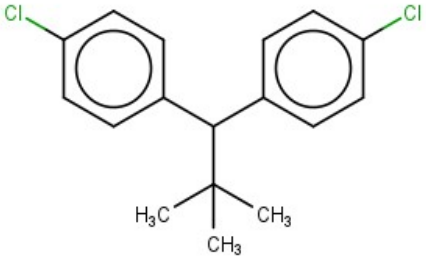
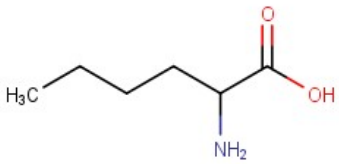
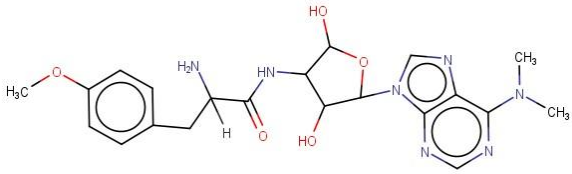
S.No	Name	Structure
1	N-[(3-chlorophenyl)methyl]-4-hydroxy-1-[2-(3-methyl-1,2-oxazol-5-yl)acetyl]pyrrolidine-2-carboxamide	
2	1-{2-[(1-cyanocyclopropyl)formamido]-3,3-dimethylbutanoyl}-4-hydroxy-N-{[4-(4-methyl-1,3-thiazol-5-yl)phenyl]methyl}pyrrolidine-2-carboxamide	
3	1-{2-[(1-acetylazetidin-3-yl)formamido]-3,3-dimethylbutanoyl}-4-hydroxy-N-{[4-(4-methyl-1,3-thiazol-5-yl)phenyl]methyl}pyrrolidine-2-carboxamide	
4	N'-[(E)-(4-ethoxy-3-methoxyphenyl)methylidene]-2-(2-{[3-(trifluoromethyl)phenyl]methyl}-1,3-thiazol-4-yl)acetohydrazide	
5	N,N'-bis(5-methyl-4-phenyl-1,3-thiazol-2-yl)pentanediamide	
6	2-(naphthalen-2-yloxy)-N-{2-[2-(naphthalen-2-yloxy)acetamido]ethyl}acetamide	

7	2-({5-ethyl-8-oxo-2H,5H,8H-[1,3]dioxolo[4,5-g]quinolin-7-yl}formamido)-N-[(furan-2-yl)methyl]-4-methylpentanamide	
8	2-{[2-amino-5-cyano-6-(methylsulfanyl)pyrimidin-4-yl]sulfanyl}-N-(3,4-dimethoxyphenyl)acetamide	
9	2-({4-amino-3-oxo-8-thia-4,6-diazatricyclo[7.4.0.0^{2,7}]trideca-1(9),2(7),5-trien-5-yl}sulfanyl)-N-(4-sulfamoylphenyl)acetamide	
10	N-(4-bromo-2-fluorophenyl)-2-({[methyl({2-[(2-methylphenyl)formamido]ethyl})amino]methyl}sulfanyl)acetamide	
11	3-{N'-[(1E)-1-(4-bromophenyl)ethylidene]hydrazinecarbonyl}-N-(2,5-dimethylphenyl)propanamide	
12	2-({6-[2-(1,3-benzodiazol-2-ylsulfanyl)acetamido]-1,3-benzothiazol-2-yl}sulfanyl)-N,N-diethylacetamide	
13	2-(4-chlorophenoxy)-N-({N'-[(E)-(9-ethyl-9H-carbazol-3-yl)methylidene]hydrazinecarbonyl}methyl)acetamide	

14	2-[(1-benzyl-4-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)formamido]acetic acid	
15	1-(2-acetamido-3,3-dimethylbutanoyl)-4-hydroxy-N-{[4-(4-methyl-1,3-thiazol-5-yl)phenyl]methyl}pyrrolidine-2-carboxamide	
16	4-hydroxy-1-(2-{[(2Z)-2-[(3-methoxyphenyl)methylidene]-3-oxo-2,3-dihydro-1-benzofuran-6-yl]oxy}acetyl)pyrrolidine-2-carboxylic acid	
17	2-(3-amino-2-methylbenzoyl)-4-hydroxy-N-{[4-(4-methyl-1,3-thiazol-5-yl)phenyl]methyl}cyclopentane-1-carboxamide	
18	2-phenylpyridine	
19	1-phenyl-1H-pyrazole	

20	benzo[h]quinoline	
21	2,2'-bipyridine	
22	2-[(4-hydroxy-1-methyl-7-phenoxy isoquinolin-3-yl)formamido]acetic acid	
23	benzyl N-[3-methyl-1-({3-methyl-1-[(4-methyl-1-oxopentan-2-yl)carbamoyl]butyl}carbamoyl)butyl]carbamate	
24	1-(2-acetamido-3,3-dimethylbutanoyl)-4-hydroxy-N-{[4-(4-methyl-1,3-thiazol-5-yl)phenyl]methyl}pyrrolidine-2-carboxamide	
25	N-{5,14,15,16-tetramethoxy-6-oxotricyclo[10.5.0.0^{2,8}]heptadeca-1(12),2,4,7,13,16-hexaen-9-yl}acetamide	

26	1-(naphthalen-1-yloxy)-3-[(propan-2-yl)amino]propan-2-ol	
27	5-{2-oxo-hexahydro-1H-thieno[3,4-d]imidazol-4-yl}pentanoic acid	
28	indole	
29	2-(2,3-dioxoaziridin-1-yl)acetic acid	
30	3,5,7-trimethyl-3H,3aH,4H,5H,6H,7H,7aH-4lambda5-imidazo[4,5-b]pyrazine-4,6-dione	
31	1-hydroxypyrrolidine-2-carboxylic acid	

32	1-phenylpentan-1-one	
33	1-chloro-4-[1-(4-chlorophenyl)-2,2-dimethylpropyl]benzene	
34	2-aminohexanoic acid	
35	2-amino-N-{5-[6-(dimethylamino)-9H-purin-9-yl]-2,4-dihydroxyoxolan-3-yl}-3-(4-methoxyphenyl)propanamide	

Supplementary Table 2. ADME properties of top hits.

Molecule	MW	XLOGP3	GI absorption	BBB permeant	CYP2D6 inhibitor	Lipinski #violations	Bioavailability Score
ZINC12529886	416.45	4.23	High	Yes	Yes	0	0.55
ZINC12892556	420.46	1.49	High	No	Yes	0	0.55
ZINC05932590	421.49	5.52	High	No	Yes	0	0.55
ZINC08765120	375.37	0.78	High	No	No	0	0.55
ZINC13690996	403.47	5.16	High	Yes	No	0	0.55
ZINC15672046	451.44	2.87	High	No	Yes	0	0.55
ZINC05397553	443.48	1.87	High	No	No	0	0.55
ZINC20113052	478.5	3.14	High	No	No	0	0.55
ZINC49543335	491.92	4.64	High	No	No	0	0.55
ZINC15959407	469.87	0.81	High	No	Yes	0	0.55
ZINC12884117	464.52	3.78	High	No	Yes	0	0.55
ZINC20757510	432.47	2.2	High	No	No	0	0.55
ZINC30903975	432.47	1.71	High	No	Yes	0	0.55
ZINC20610967	468.89	0.07	High	No	No	0	0.55
ZINC14687899	391.47	2.86	High	No	Yes	0	0.55

Supplementary Table 3. Toxicity properties of top hits.

ID	Algae at	Ames test	Daphnia at	hERG inhibition	TA1535_10RLI	TA1535_NA
ZINC12529886	0.0188155	mutagen	0.0215403	Medium	negative	Negative

				risk		
ZINC12892556	0.0591918	mutagen	0.156783	Medium risk	negative	Negative
ZINC05932590	0.0186102	mutagen	0.0276657	ambiguous	negative	Negative
ZINC08765120	0.0966894	mutagen	0.679164	medium risk	negative	Negative
ZINC13690996	0.0270726	non-mutagen	0.103963	Medium risk	negative	Negative
ZINC15672046	0.0134879	mutagen	0.0537564	Medium risk	positive	Negative
ZINC05397553	0.0405294	mutagen	0.0553373	Low risk	negative	Negative
ZINC20113052	0.0221285	non-mutagen	0.17078	Medium risk	negative	Negative
ZINC49543335	0.0110922	mutagen	0.0182689	Medium risk	negative	Negative
ZINC15959407	0.0636452	non-mutagen	0.527895	Low risk	negative	Negative
ZINC12884117	0.0149674	mutagen	0.0424046	Low risk	negative	Negative
ZINC20757510	0.0337373	mutagen	0.195727	High risk	negative	Negative
ZINC30903975	0.101538	non-mutagen	0.890035	Medium risk	negative	Negative
ZINC20610967	0.124541	non-mutagen	1.02373	High risk	negative	Negative
ZINC14687899	0.0955258	mutagen	0.18622	High risk	negative	Negative