

Supplementary Table S1. Characterization and database information of standards and natural compounds from *Vitex trifolia*

Compound no.	Compound Name	Identifier		
		PubChem /ChemSpider CID	SMILES	PubChem /ChemSpider Link
—	Quercetin	5280343	<chem>C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/5280343
—	Gallic Acid	370	<chem>C1=C(C=C(C(=C1O)O)O)C(=O)O</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/370
Compound 1	Casticin (NP-001928)	5315263	<chem>COC1=C(C=C(C=C1)C2=C(C(=O)C3=C(C(=C(C=C3O2)OC)OC)O)OC)O</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/5315263
Compound 2	(1 <i>ξ</i>)-1,5-Anhydro-1-[2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4H-chromen-8-yl]-D-galactitol	22912936	<chem>O[C@@H]1[C@H]([C@H]([C@@H](CO)OC1C1=C2C(C(C=C(C3=CC=C(O)C(O)=C3)O2)=O)=C(O)C=C1O)O)O</chem>	https://www.chemspider.com/Chemical-Structure.22912936.html
Compound 3	(2 <i>S</i> ,3 <i>S</i> ,4 <i>S</i> ,5 <i>R</i> ,6 <i>S</i>)-6-[[5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl]oxy]-3,4,5-trihydroxyoxane-2-carboxylic acid	57509403	<chem>C[C@H]1[C@@H]([C@H]([C@H]([C@@H](O1)O[C@@H]2[C@H]([C@@H]([C@H](O[C@H]2OC3=C(OC4=CC(=CC(=C4C3=O)O)O)C5=CC=C(C=C5)O)C(=O)O)O)O)O)O</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/57509403
Compound 4	5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-3,6-dimethoxy-4H-chromen-4-one	4474997	<chem>C12C(O)=C(OC)C(=CC=1OC(=C(OC)C2=O)C1=CC=C(C(O)=C1)OC)O</chem>	https://www.chemspider.com/Chemical-Structure.4474997.html
Compound 5	4-Coumaric acid	322	<chem>C1=CC(=CC=C1C=CC(=O)O)O</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/322

Compound 6	(1R,3R,4R,4aS)-4-Hydroxy-3,4a,8,8-tetramethyl-4-[2-(5-oxo-2,5-dihydro-3-furanyl)ethyl]decahydro-1-naphthalenyl acetate	22913002	<chem>O(C(=O)C)[C@@H]1C[C@@H](C)[C@@](O)([C@@]2(C1C(C)(C)CCC2)C)CCC1COC(=O)C=1</chem>	https://www.chemspider.com/Chemical-Structure.22913002.html
Compound 7	(1r,3R,4s,5S)-4-[[[(2E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy]-1,3,5-trihydroxycyclohexane-1-carboxylic acid	29814674	<chem>O[C@H]1C[C@@](O)(C[C@@H](O)[C@H]1OC(=O)\C=C\C1=CC=C(O)C(O)=C1)C(O)=O</chem>	https://www.chemspider.com/Chemical-Structure.29814674.html
Compound 8	(1S,3R,4S,5R)-3,5-bis([[(2E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy])-1,4-dihydroxycyclohexane-1-carboxylic acid	22912767	<chem>[C@@H]1(OC(=O)C=CC2C=CC(O)=C(O)C=2)C[C@](C[C@@H](OC(=O)C=CC2=CC=C(O)C(O)=C2)[C@H]1O)(O)C(=O)O</chem>	https://www.chemspider.com/Chemical-Structure.22912767.html
Compound 9	Lupeol	259846	<chem>CC(=C)[C@@H]1CC[C@]2([C@H]1[C@H]3CC[C@@H]4[C@]5(CC[C@@H](C([C@@H]5)CC[C@]4([C@@]3(CC2)C)C)(C)C)O)C)C</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/259846
Compound 10	4-Hydroxybenzoic acid	135	<chem>C1=CC(=CC=C1C(=O)O)O</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/135
—	Batimastat (Collagenase Standard)	5362422	<chem>CC(C)C[C@H]([C@H](CSC1=CC=CS1)C(=O)NO)C(=O)N[C@@H](CC2=CC=CC=C2)C(=O)NC</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/5362422
—	Baicalain (Elastase Standard)	5281605	<chem>C1=CC=C(C=C1)C2=CC(=O)C3=C(O2)C=C(C(=C3O)O)O</chem>	https://pubchem.ncbi.nlm.nih.gov/compound/5281605

Supplementary Table S2. Toxicity prediction of compounds detected in *Vitex trifolia* using ProTox-II

Compound no.	Compound name	Toxicity class	LD ₅₀ * (mg/kg)	Accuracy (%)	Hepatotoxicity	Immunotoxicity	Carcinogenicity	Mutagenicity
—	Quercetin	3	159	100	Inactive (0.69)	Inactive (0.87)	<u>Active (0.68)</u>	<u>Active (0.51)</u>
—	Gallic Acid	4	2000	70.97	Inactive (0.61)	Inactive (0.99)	<u>Active (0.56)</u>	Inactive (0.94)
Compound 1	Casticin (NP-001928)	5	5000	72.9	Inactive (0.70)	<u>Active (0.98)</u>	Inactive (0.63)	Inactive (0.77)
Compound 2	(1 <i>ξ</i>)-1,5-Anhydro-1-[2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4H-chromen-8-yl]-D-galactitol	4	1213	67.38	Inactive (0.81)	<u>Active (0.52)</u>	Inactive (0.72)	<u>Active (0.52)</u>
Compound 3	(2 <i>S</i> ,3 <i>S</i> ,4 <i>S</i> ,5 <i>R</i> ,6 <i>S</i>)-6-{[5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl]oxy}-3,4,5-trihydroxyoxane-2-carboxylic acid	5	5000	70.97	Inactive (0.75)	<u>Active (0.98)</u>	Inactive (0.55)	Inactive (0.63)
Compound 4	5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-3,6-dimethoxy-4H-chromen-4-one	5	5000	70.97	Inactive (0.70)	<u>Active (0.97)</u>	Inactive (0.69)	Inactive (0.82)
Compound 5	4-Coumaric acid	5	2850	100	Inactive (0.51)	Inactive (0.91)	<u>Active (0.50)</u>	Inactive (0.93)
Compound 6	(1 <i>R</i> ,3 <i>R</i> ,4 <i>R</i> ,4 <i>aS</i>)-4-Hydroxy-3,4 <i>a</i> ,8,8-tetramethyl-4-[2-(5-oxo-2,5-dihydro-3-furanyl)ethyl]decahydro-1-naphthalenyl acetate	2	34	72.9	Inactive (0.83)	<u>Active (0.97)</u>	Inactive (0.55)	Inactive (0.90)
Compound 7	(1 <i>r</i> ,3 <i>R</i> ,4 <i>s</i> ,5 <i>S</i>)-4-{[(2 <i>E</i>)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy}-1,3,5-trihydroxycyclohexane-1-	5	5000	69.26	Inactive (0.72)	<u>Active (0.99)</u>	Inactive (0.68)	Inactive (0.93)

	carboxylic acid							
Compound 8	(1S,3R,4S,5R)-3,5-bis([[(2E)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy])-1,4-dihydroxycyclohexane-1-carboxylic acid	5	5000	69.26	Inactive (0.70)	<u>Active (0.99)</u>	Inactive (0.63)	Inactive (0.85)
Compound 9	Lupeol	4	2000	100	Inactive (0.91)	<u>Active (0.57)</u>	Inactive (0.63)	Inactive (0.95)
Compound 10	4-Hydroxybenzoic acid	5	2200	100	Inactive (0.52)	Inactive (0.99)	Inactive (0.51)	Inactive (0.99)

*Class I: fatal if swallowed ($LD_{50} \leq 5$), Class II: fatal if swallowed ($5 < LD_{50} \leq 50$), Class III: toxic if swallowed ($50 < LD_{50} \leq 300$), Class IV: harmful if swallowed ($300 < LD_{50} \leq 2000$), Class V: may be harmful if swallowed ($2000 < LD_{50} \leq 5000$), Class VI: non-toxic ($LD_{50} > 5000$).

Supplementary Table S3. *In silico* drug-likeness assessment of natural compounds using Lipinski's and Veber's rules

Compound no.	Compound Name	Lipinski's rule				Veber's rule		Lipinski's Violation	Veber's Violation
		MW (≤ 500 Da)	HBD (≤ 5)	HBA (≤ 10)	M ^{logP} (≤ 4.15)	RB (≤ 10)	TPSA (< 140 Å)		
—	Quercetin	302.24	5	7	-0.56	1	131.36	0	0
—	Gallic Acid	170.12	4	5	-0.16	1	97.99	0	0
Compound 1	Casticin (NP-001928)	374.34	2	8	-0.12	5	107.59	0	0
Compound 2	(1 <i>ξ</i>)-1,5-Anhydro-1-[2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4H-chromen-8-yl]-D-galactitol	448.38	8	11	-2.51	3	201.28	2	1
Compound 3	(2 <i>S</i> ,3 <i>S</i> ,4 <i>S</i> ,5 <i>R</i> ,6 <i>S</i>)-6-[[5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl]oxy]-3,4,5-trihydroxyoxane-2-carboxylic acid	608.5	9	16	-3.42	6	266.27	3	1
Compound 4	5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-3,6-dimethoxy-4H-chromen-4-one	360.31	3	8	-0.35	4	118.59	0	0
Compound 5	4-Coumaric acid	164.16	2	3	1.28	2	57.53	0	0
Compound 6	(1 <i>R</i> ,3 <i>R</i> ,4 <i>R</i> ,4 <i>aS</i>)-4-Hydroxy-3,4 <i>a</i> ,8,8-tetramethyl-4-[2-(5-oxo-2,5-dihydro-3-furanyl)ethyl]decahydro-1-naphthalenyl acetate	378.5	1	5	3.23	5	72.83	0	0
Compound 7	(1 <i>r</i> ,3 <i>R</i> ,4 <i>s</i> ,5 <i>S</i>)-4-[[[(2 <i>E</i>)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy]-1,3,5-trihydroxycyclohexane-1-carboxylic acid	354.31	6	9	-1.05	5	164.75	1	1
Compound 8	(1 <i>S</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-3,5-bis([[[(2 <i>E</i>)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy]])-1,4-dihydroxycyclohexane-1-carboxylic acid	516.45	7	12	-0.35	9	211.28	3	1
Compound 9	Lupeol	426.72	1	1	6.92	1	20.23	1	0
Compound 10	4-Hydroxybenzoic acid	138.12	2	3	0.99	1	57.53	0	0

Supplementary Table S4. Binding affinity of different standards and natural compounds found in *Vitex trifolia* against MMP9 and elastase

Compound no.	Compound Name	Binding affinity (Kcal/mol)	
		MMP-9	Elastase
—	Quercetin	-6.687	-6.065
—	Gallic Acid	-6.881	-4.664
Compound 1	Casticin (NP-001928)	-5.85	-5.059
Compound 2	(1 <i>ξ</i>)-1,5-Anhydro-1-[2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4-oxo-4H-chromen-8-yl]-D-galactitol	-1.77	-3.647
Compound 3	(2 <i>S</i> ,3 <i>S</i> ,4 <i>S</i> ,5 <i>R</i> ,6 <i>S</i>)-6-[[5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4H-chromen-3-yl]oxy]-3,4,5-trihydroxyoxane-2-carboxylic acid	19.259	-4.923
Compound 4	5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-3,6-dimethoxy-4H-chromen-4-one	-6.368	-5.341
Compound 5	4-Coumaric acid	-7.077	-5.169
Compound 6	(1 <i>R</i> ,3 <i>R</i> ,4 <i>R</i> ,4 <i>aS</i>)-4-Hydroxy-3,4 <i>a</i> ,8,8-tetramethyl-4-[2-(5-oxo-2,5-dihydro-3-furanyl)ethyl]decahydro-1-naphthalenyl acetate	-0.593	-5.238
Compound 7	(1 <i>r</i> ,3 <i>R</i> ,4 <i>s</i> ,5 <i>S</i>)-4-[[[(2 <i>E</i>)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy]-1,3,5-trihydroxycyclohexane-1-carboxylic acid	-8.108	-5.984
Compound 8	(1 <i>S</i> ,3 <i>R</i> ,4 <i>S</i> ,5 <i>R</i>)-3,5-bis({[(2 <i>E</i>)-3-(3,4-dihydroxyphenyl)prop-2-enoyl]oxy})-1,4-dihydroxycyclohexane-1-carboxylic acid	-6.782	-4.566
Compound 9	Lupeol	-5.267	-3.643
Compound 10	4-Hydroxybenzoic acid	-5.462	-4.273
—	Batimastat (collagenase standard)	-2.739	-
—	Baicalain (elastase standard)	-	-6.248