

Supplementary materials

Table S1 Sequence of primers used in quantitative RT-PCR

Gene	Accession number	Forward primers (5'-3')	Reverse primers(5'-3')
PPAR γ	NM_001127330.2	CGCTGATGCACTGCCTATGA	AGAGGTCCACAGAGCTGATTCC
β -actin	NM_007393.5	ACTGCTCTGGCTCCTAGCAC	CCACCGATCCACACAGAGTA

Table S2 The explored candidates based on genistein

Name	Score	SMILES format
ZINC18825330(genistein)	0.994	<chem>Oc1ccc(cc1)c1coc2c(c1=O)c(O)cc(c2)O</chem>
ZINC06525249	0.988	<chem>Oc1ccc(c(c1)O)c1coc2c(c1=O)c(O)cc(c2)O</chem>
ZINC00391976	0.987	<chem>Oc1ccc2c(c1)occ(c2=O)c1ccc(c(c1)O)O</chem>
ZINC06525252	0.985	<chem>Oc1ccc(c(c1)O)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC06092209	0.984	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1ccc(c(c1)O)O</chem>
ZINC02392251	0.981	<chem>Oc1cccc(c1)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC00391977	0.981	<chem>Oc1ccc(cc1)c1coc2c(c1=O)cc(c(c2)O)O</chem>
ZINC02149675	0.975	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1cccc1</chem>
ZINC34259774	0.972	<chem>Oc1ccc(cc1)c1cc2c(O)cc(cc2oc1=O)O</chem>
ZINC06093399	0.969	<chem>Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2O)O</chem>
ZINC18847034	0.965	<chem>Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC18847037	0.949	<chem>COc1ccc(cc1)c1coc2c(c1=O)c(O)cc(c2)O</chem>
ZINC02561259	0.946	<chem>COc1cc(ccc1O)c1coc2c(c1=O)c(O)cc(c2)O</chem>
ZINC00304562	0.939	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1ccc(cc1)Br</chem>
ZINC28631041	0.932	<chem>Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2C)O</chem>
ZINC05999775	0.931	<chem>Oc1cc2occ(c(=O)c2cc1O)c1cccc1</chem>
ZINC05731331	0.93	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1cccc1F</chem>
ZINC14924498	0.929	<chem>Oc1ccc(cc1O)c1coc2c(c1=O)c(O)cc(c2Cl)O</chem>
ZINC05997152	0.929	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1ccc(cc1)F</chem>
ZINC06484607	0.928	<chem>COc1ccc(cc1O)c1coc2c(c1=O)c(O)cc(c2)O</chem>
ZINC05731170	0.926	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1ccc(cc1)Cl</chem>
ZINC06484559	0.922	<chem>COc1ccc(cc1)c1coc2c(c1=O)cc(c(c2)O)O</chem>
ZINC14758993	0.92	<chem>COc1cc(O)cc2c1c(=O)c(co2)c1ccc(cc1O)O</chem>
ZINC05730173	0.919	<chem>Oc1cc(O)c2c(c1)oc(c(c2=O)c1cccc1)C</chem>
ZINC06018563	0.919	<chem>COc1ccc(cc1O)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC14982695	0.917	<chem>Oc1cc(O)c2c(c1)oc(=O)c(c2)c1cccc1</chem>
ZINC94993400	0.905	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1cccc1Cl</chem>
ZINC13124366	0.903	<chem>COc1cc(O)cc2c1c(=O)c(co2)c1ccc(cc1)O</chem>
ZINC00899915	0.897	<chem>COc1c(O)cc2c(c1O)c(=O)c(co2)c1ccc(cc1)O</chem>
ZINC03874807	0.885	<chem>COc1c(O)cc(c2c1occ(c2=O)c1ccc(cc1)O)O</chem>
ZINC20272107	0.88	<chem>Nc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC38418848	0.873	<chem>Oc1ccc(cc1)c1cc2ccc(cc2oc1=O)O</chem>
ZINC94993451	0.854	<chem>Oc1cc(O)c2c(c1)oc(c(c2=O)c1ccc(cc1)Cl)C</chem>
ZINC18847036	0.852	<chem>COc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC12428608	0.847	<chem>Oc1ccc(cc1)c1coc2c(c1=O)c(O)ccc2</chem>
ZINC06556138	0.843	<chem>COc1cccc1c1coc2c(c1=O)c(O)cc(c2)O</chem>
ZINC06484558	0.84	<chem>COc1ccc(cc1)c1coc2c(c1=O)c(O)c(c(c2)O)OC</chem>

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ZINC08015480	0.833	Oc1ccc(cc1)c1c(C)oc2c(c1=O)ccc(c2)O
ZINC14759160	0.832	COc1ccc(cc1O)c1coc2c(c1=O)cc(c(c2)O)OC
ZINC05999205	0.83	COc1cc2c(cc1O)occ(c2=O)c1ccc(cc1)O
ZINC08379245	0.819	[O-][N+](=O)c1ccc(cc1)c1coc2c(c1=O)ccc(c2O)O
ZINC13518422	0.813	Oc1ccc2c(c1)occ(c2=O)c1ccccc1
ZINC05010172	0.805	Oc1ccc2c(c1)occ(c2=O)c1ccc(cc1)[N+](=O)[O-]
ZINC03871576	0.794	Oc1ccc(cc1)c1cc(=O)c2c(o1)cc(cc2O)O
ZINC05765089	0.792	Oc1cc(C)c2c(c1)oc1c(c2=O)c(O)cc(c1)O
ZINC06556398	0.789	COc1ccc(cc1)c1c(C)oc2c(c1=O)c(O)cc(c2)O
ZINC02559341	0.78	COc1cc(O)ccc1c1coc2c(c1=O)ccc(c2)O
ZINC06557424	0.776	Fc1ccc(cc1)c1coc2c(c1=O)ccc(c2O)O
ZINC14761282	0.763	Oc1cc(O)c2c(c1)oc1c(c2=O)c(C)c(c(c1)O)O
ZINC06556311	0.758	Oc1ccc2c(c1C)occ(c2=O)c1ccccc1
ZINC02131332	0.757	Oc1ccc2c(c1)oc(=O)c(c2)c1cc(=O)oc2c1ccc(c2O)O
ZINC94993418	0.757	OCc1c(O)ccc2c1occ(c2=O)c1ccccc1F
ZINC14759216	0.756	COc1ccc(cc1O)c1coc2c(c1=O)ccc(c2OC)O
ZINC13555056	0.753	Oc1ccc(cc1)c1coc2c(c1=O)cccc2
ZINC71405008	0.753	Oc1ccc(cc1)c1coc2c(c1=O)c1ccccc1cc2
ZINC18185774	0.752	Oc1cc(O)c2c(c1)oc(cc2=O)c1ccc(c(c1)O)O
ZINC02573898	0.751	Oc1cc(O)c2c(c1)oc(=O)c(c2C)c1ccccc1
ZINC18847044	0.747	COc1cc(O)c2c(c1)occ(c2=O)c1ccc(cc1)O
ZINC06534275	0.746	Oc1cc(O)c2c(c1)occ(c2=O)c1ccccc1
ZINC57312208	0.743	OCc1c(O)ccc2c1occ(c2=O)c1ccc(cc1)F
ZINC06557553	0.736	Clc1ccccc1c1coc2c(c1=O)ccc(c2O)O
ZINC06556076	0.735	COc1cc(ccc1OC)c1coc2c(c1=O)c(O)cc(c2)O
ZINC17887543	0.731	Oc1ccc2c(c1)oc(cc2=O)c1cc(O)c(c(c1)O)O
ZINC06018481	0.729	COc1ccc(cc1)c1coc2c(c1=O)c(O)cc(c2)OC
ZINC64219018	0.724	Cc1cc(O)c2c(c1)occ(c2=O)c1ccc(cc1)O
ZINC00968077	0.724	COc1ccc2c(c1)occ(c2=O)c1ccc(cc1)O
ZINC05731171	0.724	BrC1ccc(cc1)c1coc2c(c1=O)ccc(c2)O
ZINC18847051	0.72	Oc1ccc2c(c1)occ(c2=O)c1ccc2c(c1)OCO2
ZINC05730178	0.712	Cc1oc2c(O)c(O)ccc2c(=O)c1c1ccccc1
ZINC00057588	0.704	COc1ccc(cc1)c1coc2c(c1=O)ccc(c2)OC
ZINC00058170	0.69	COc1ccc(cc1)c1coc2c(c1=O)c(OC)cc(c2)OC
ZINC02566738	0.69	COc1cc(OC)cc2c1c(=O)c(co2)c1ccccc1
ZINC11865257	0.69	COc1cc(OC)cc2c1c(=O)c(co2)c1ccc(cc1)O
ZINC11865149	0.684	COc1ccc(cc1)c1coc2c(c1=O)ccc(c2C)O
ZINC00046554	0.678	COc1ccc2c(c1)occ(c2=O)c1ccccc1
ZINC05817433	0.664	CC(Oc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O)C
ZINC05732527	0.657	COc1cc(cc(c1OC)O)c1coc2c(c1=O)c(O)c(c(c2)O)OC
ZINC14761164	0.654	Oc1ccc(cc1O)c1cc(=O)c2c(o1)cc(c(c2O)C)O
ZINC02553970	0.648	COc1cc2c(cc1O)occ(c2=O)c1ccc(cc1)OC(=O)C
ZINC02576403	0.644	CCOc1ccc2c(c1)occ(c2=O)c1ccc(cc1)O
ZINC02545404	0.636	Oc1cc(C)c2c(c1)occ(c2=O)c1ccccc1

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ZINC00307531	0.636	<chem>Fc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC05731172	0.636	<chem>Clc1ccc(cc1)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC05817431	0.631	<chem>CC(Oc1cc(O)c2c(c1)occ(c2=O)c1ccc(cc1)O)C</chem>
ZINC48057119	0.624	<chem>Oc1ccc(cc1)c1coc2c(c1=O)cc(c(c2)C)C</chem>
ZINC04282141	0.624	<chem>Oc1cc(O)c2c(c1)occ(c2=O)c1ccc2c(c1)OCCO2</chem>
ZINC00134646	0.624	<chem>COc1ccc(cc1)c1coc2c(c1=O)cccc2</chem>
ZINC48057013	0.623	<chem>COc1ccc(cc1)c1coc2c(c1=O)ccc(c2C)OC</chem>
ZINC00490845	0.623	<chem>CCOc1ccc2c(c1)occ(c2=O)c1ccc(cc1)OC</chem>
ZINC02573896	0.621	<chem>COc1ccc(cc1)c1c(=O)oc2c(c1C)c(O)cc(c2)O</chem>
ZINC14811680	0.619	<chem>Oc1cc(O)c2c(c1)oc(=O)c(c2O)c1cccc1</chem>
ZINC13520048	0.615	<chem>Oc1cc(O)c2c(c1)oc(cc2=O)c1cc(O)c(c(c1)O)O</chem>
ZINC57312206	0.612	<chem>OCc1c(O)ccc2c1oc(C)c(c2=O)c1ccc(cc1)F</chem>
ZINC06796105	0.607	<chem>Fc1ccc(cc1)c1c(C)oc2c(c1=O)ccc(c2O)O</chem>
ZINC03473319	0.607	<chem>COc1ccc2c(c1)occ(c2=O)c1ccc(cc1O)O</chem>
ZINC39289884	0.607	<chem>COc1ccc2c(c1)occ(c2=O)c1cc(O)c(c(c1)O)O</chem>
ZINC05925628	0.604	<chem>Nc1ccc(cc1)c1c(C)oc2c(c1=O)ccc(c2)O</chem>
ZINC02563647	0.603	<chem>COc1ccc(cc1)c1coc2c(c1=O)cc(c(c2)OC)O</chem>
ZINC06018480	0.603	<chem>COc1ccc(cc1)c1coc2c(c1=O)cc(c(c2)O)OC</chem>
ZINC06008303	0.601	<chem>COc1cccc1c1c(C)oc2c(c1=O)c(O)cc(c2)O</chem>
ZINC02553967	0.573	<chem>COc1cc2c(cc1O)occ(c2=O)c1cccc1</chem>
ZINC00004016	0.573	<chem>CC(Oc1ccc2c(c1)occ(c2=O)c1cccc1)C</chem>
ZINC71404828	0.571	<chem>Oc1cccc(c1)c1coc2c(c1=O)ccc1c2cccc1</chem>
ZINC71404826	0.571	<chem>Oc1cccc(c1)c1coc2c(c1=O)c1cccc1cc2</chem>
ZINC14759265	0.571	<chem>COc1ccc(cc1)c1coc2c(c1=O)c(O)c(c(c2)OC)OC</chem>
ZINC00629835	0.571	<chem>CCOc1ccc(cc1)c1coc2c(c1=O)c(OCC)cc(c2)OCC</chem>
ZINC11865148	0.562	<chem>COc1ccc(cc1)c1coc2c(c1=O)c(C)cc(c2)O</chem>
ZINC05686755	0.562	<chem>CCc1cc2c(cc1O)occ(c2=O)c1ccc(cc1)OC</chem>
ZINC19703228	0.56	<chem>Oc1ccc2c(c1)occ(c2=O)c1ccc2c(c1)cc(o2)C(=O)O</chem>
ZINC05842416	0.555	<chem>Oc1ccc(cc1)c1cc(=O)c2c(o1)cc(c(c2O)O)O</chem>
ZINC06483767	0.553	<chem>Oc1cc(O)c2c(c1)oc(c(c2=O)C)C</chem>
ZINC00162916	0.553	<chem>COc1cccc(c1)c1coc2c(c1=O)ccc(c2)O</chem>
ZINC05686285	0.553	<chem>CCCc1cc2c(cc1O)occ(c2=O)c1cccc1</chem>
ZINC01081057	0.552	<chem>COc1cc(OC)cc2c1c(=O)c(co2)c1ccc(cc1)Br</chem>
ZINC00058158	0.514	<chem>COc1cc(OC)cc2c1c(=O)c(co2)c1ccc(cc1)Cl</chem>
ZINC05195795	0.514	<chem>CC(=CCc1c(O)cc2c(c1O)c(=O)c(co2)c1ccc(cc1)O)C</chem>
ZINC05730811	0.513	<chem>Oc1ccc2c(c1)oc(c(c2=O)c1cccc1C)C</chem>
ZINC02405925	0.474	<chem>N#CCOc1ccc2c(c1)occ(c2=O)c1cccc1</chem>
ZINC06090922	0.473	<chem>Oc1cc(O)c2c(c1)oc1c(c2=O)cc(c(c1)O)O</chem>
ZINC03871358	0.473	<chem>COc1ccc(cc1)c1cc(=O)c2c(o1)cc(cc2O)O</chem>
ZINC34909584	0.469	<chem>Cc1ccc(cc1)c1coc2c(c1=O)cc(cc2)C</chem>
ZINC14819517(8PG)	0.45	<chem>CC(C)=CCc1c(O)cc(O)c2c(=O)c(-c3ccc(O)cc3)coc12</chem>
ZINC06383544	0.448	<chem>COc1ccc(cc1)c1c(C)oc2c(c1=O)ccc(c2C)O</chem>
ZINC95457398	0.431	<chem>COc1ccc(cc1)c1coc2c(c1=O)ccc(c2)OCC1CCC1</chem>
ZINC11865286	0.431	<chem>Brc1ccc(cc1)c1c(=O)oc2c(c1O)ccc(c2)O</chem>

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ZINC02576376	0.431	<chem>BrCCCOc1ccc2c(c1)occ(c2=O)c1ccc(cc1)O</chem>
ZINC00384434	0.426	<chem>Oc1ccc(c(c1)O)c1cc2ccccc2oc1=O</chem>
ZINC34909566	0.426	<chem>Cc1ccc2c(c1)occ(c2=O)c1cccc1</chem>
ZINC11765878	0.425	<chem>Oc1ccc2c(c1)oc(=O)c(c2)c1ccc(cc1)OC(F)(F)F</chem>
ZINC00084913	0.425	<chem>Oc1cc(O)c2c(c1)oc(c(c2=O)c1cccc1)c1cccc1</chem>
ZINC39096796	0.42	<chem>Oc1cc2occ(c(=O)c2c(c1O)O)C</chem>
ZINC02553968	0.414	<chem>COc1ccc(cc1OC)c1coc2c(c1=O)cc(c(c2)OC)OC</chem>
ZINC00058067	0.413	<chem>Oc1ccc2c(c1)oc(=O)c(c2C)c1cccc1</chem>
ZINC32558314	0.413	<chem>OCc1ccc(cc1)c1coc2c(c1=O)cccc2</chem>
ZINC57312204	0.409	<chem>CN(Cc1c(O)ccc2c1occ(c2=O)c1ccc(cc1)F)C</chem>
ZINC05854353	0.409	<chem>CC(=CCc1c(O)cc2c(c1O)c(=O)c(co2)c1ccc(cc1O)O)C</chem>
ZINC00491307	0.402	<chem>CC(=C)COc1ccc2c(c1)occ(c2=O)c1cccc1</chem>
ZINC02573935	0.401	<chem>Oc1ccc(cc1)c1c(=O)oc2c(c1C)cccc2</chem>
ZINC00057658	0.4	<chem>Oc1ccc(cc1)c1cc(=O)c2c(o1)cc(cc2)O</chem>

Table S3 Summary of the bone protective effects and potential targets of 8PG and genistein.

cell type	Osteoprotective activity		Mechanism of action		
	Activity type	8PG	genistein	8PG	genistein
pre-adipocyte (3T3-L1)	adipocyte			FASN↓	FASN↓
	differentiation	↓	↓	Wnt/β-catenin pathway↑	Wnt/β-catenin pathway↑

↓: inhibited; ↑ promoted.