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Supplementary information to:

RATIONAL DESIGN OF NOVEL COUMARINS: A POTENTIAL TREND FOR ANTIOXIDANTS IN COSMETICS

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Supplementary Table 1: Intercorrelation matrix of significant molecular descriptors from Dragon software

	nArNHR	ISH	B04[O-O]	G2p
nArNHR	1.000			
ISH	-0.173	1.000		
B04[O-O]	-0.592	0.233	1.000	
G2p	0.089	0.176	-0.229	1.000

Supplementary Table 2: Intercorrelation matrix of significant molecular descriptors from Mold^2 software

	D491	D278	D467	D384	D580	D461
D491	1.000					
D278	0.117	1.000				
D467	-0.502	0.096	1.000			
D384	-0.198	0.189	0.262	1.000		
D580	-0.108	0.223	-0.121	-0.123	1.000	
D461	0.466	0.19	-0.508	-0.016	-0.442	1.000

Supplementary Table 3: Intercorrelation matrix of significant molecular descriptors from PaDEL software

	SHBint4	SpMin2_Bhe	MATS8e	SssCH2
SHBint4	1.000			
SpMin2_Bhe	-0.485	1.000		
MATS8e	-0.018	0.167	1.000	
SssCH2	0.303	-0.857	-0.01	1.000

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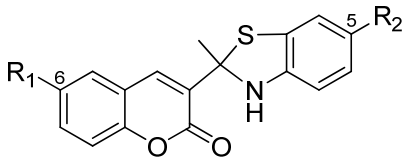
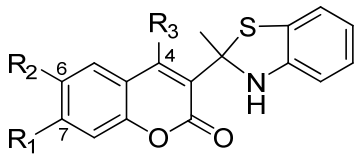
Supplementary Table 4: Rational designed chemical structures of 69 new coumarin derivatives



2a-2h

Compound	R_1	R_2	Predicted antioxidant activity (pIC_{50})		
			Model 1	Model 2	Model 3
2a	-H	-F	3.667	3.776	3.498
2b	-H	$-CF_3$	3.861	3.662	4.503
2c	-H	$-NO_2$	3.634	3.724	4.189
2d	$-NO_2$	-F	3.828	3.745	3.564
2e	$-NO_2$	$-CF_3$	3.801	3.625	4.502
2f	$-NO_2$	-Cl	3.828	3.289	3.401
2g	-CN	-Cl	3.743	3.459	3.371
2h	$-CF_3$	-Cl	3.716	3.167	3.378



3a-3p

Compound	R_1	R_2	R3	Predicted antioxidant activity (pIC_{50})		
				Model 1	Model 2	Model 3
3a	-H	-Cl	-H	3.740	3.148	4.025
3b	-H	-F	-H	3.788	4.089	4.141
3c	-H	$-CF_3$	-H	3.756	3.849	3.477
3d	-H	$-NO_2$	-H	3.829	3.968	3.583
3e	-H	-CN	-H	3.546	4.140	3.741
3f	-OH	-Br	-H	4.075	4.575	4.564
3g	$-OCH_3$	-Br	-H	4.379	3.595	3.879
3h	$-NH_2$	-Br	-H	3.508	4.600	4.593
3i	$-N(CH_3)_2$	-Br	-H	3.878	3.277	3.991
3j	-SH	-Br	-H	3.811	4.537	4.588
3k	$-S(C_6H_5)$	-Br	-H	3.735	4.129	3.905
3l	-H	-Br	-OH	4.098	4.132	4.852
3m	-H	-Br	$-OCH_3$	3.791	3.017	4.352
3n	-H	-Br	$-NH_2$	3.660	4.182	6.340
3o	-H	-Br	$-N(CH_3)_2$	3.675	2.804	3.920
3p	$-OCH_3$	-Br	$-OCH_3$	4.451	2.948	4.491

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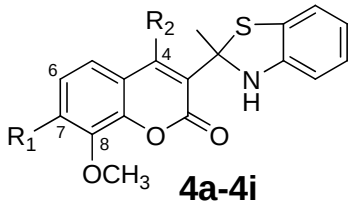
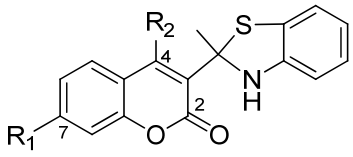
Supplementary Table 4 (cont.): Rational designed chemical structures of 69 new coumarin derivatives



4a-4i

Compound	R_1	R_2	Predicted antioxidant activity activity (pIC_{50})		
			Model 1	Model 2	Model 3
4a	-OH	-H	4.286	4.362	4.729
4b	$-OCH_3$	-H	4.040	3.717	3.978
4c	$-NH_2$	-H	4.033	4.371	4.772
4d	$-N(CH_3)_2$	-H	3.551	3.577	4.051
4e	-H	-OH	4.306	3.830	4.924
4f	-H	$-OCH_3$	3.998	2.865	4.423
4g	-H	$-NH_2$	4.139	3.746	6.445
4h	-H	$-N(CH_3)_2$	3.456	2.601	3.969
4i	$-OCH_3$	$-OCH_3$	4.095	2.931	4.533



5a-5l

Compound	R_1	R_2	Predicted antioxidant activity (pIC_{50})		
			Model 1	Model 2	Model 3
5a	$-OCH_3$	-H	4.219	3.567	3.796
5b	$-NH_2$	-H	3.802	4.579	4.518
5c	-SH	-H	3.875	4.534	4.463
5d	-OH	$-CH_3$	3.804	3.705	4.410
5e	-OH	$- C_6H_5$	4.003	3.930	4.452
5f	-OH	$-OCH_3$	4.130	3.626	5.123
5g	-OH	-OH	4.223	4.495	5.466
5h	-OH	$-NH_2$	3.924	4.503	7.016
5i	-OH	$-N(CH_3)_2$	3.923	3.327	4.745
5j	$-OCH_3$	$-OCH_3$	3.892	3.517	3.055
5k	$-N(CH_3)_2$	-H	4.060	3.214	3.925
5l	$-S(C_6H_5)$	-H	3.739	4.130	3.813

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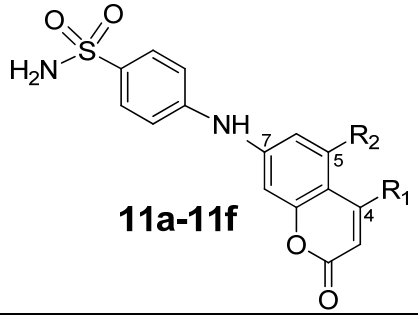
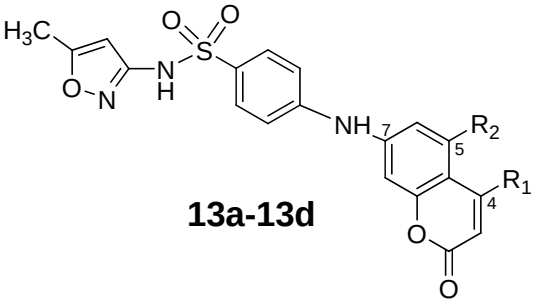
Supplementary Table 4 (cont.): Rational designed chemical structures of 69 new coumarin derivatives



11a-11f

Compound	R_1	R_2	Predicted antioxidant activity (pIC_{50})		
			Model 1	Model 2	Model 3
11a	$-CH_3$	-H	3.582	4.526	3.708
11b	$-OCH_3$	-H	4.085	3.705	3.758
11c	$-C_6H_5$	-H	3.402	4.110	3.966
11d	$-OC_6H_5$	-H	4.198	4.317	3.775
11e	$-CH_3$	$-CH_3$	3.644	3.829	3.702
11f	$-OCH_3$	$-OCH_3$	3.970	2.610	4.364



13a-13d

Compound	R_1	R_2	Predicted antioxidant activity (pIC_{50})		
			Model 1	Model 2	Model 3
13a	$-CH_3$	$-CH_3$	3.401	3.528	3.742
13b	-OH	$-CH_3$	4.035	3.903	3.607
13c	$-OCH_3$	$-CH_3$	4.076	3.341	3.762
13d	$-OCH_3$	$-OCH_3$	4.007	2.642	4.356

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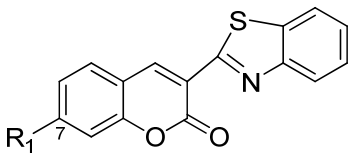
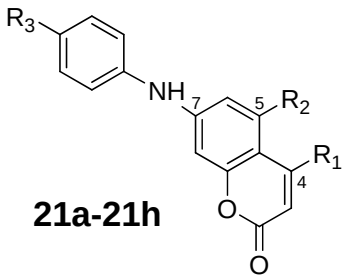


18a-18f

Compound	R_1	Predicted antioxidant activity (pIC_{50})		
		Model 1	Model 2	Model 3
18a	$-OCH_3$	2.958	2.820	3.037
18b	-OH	3.468	3.983	3.773
18c	$-NH_2$	2.941	4.197	3.798
18d	-SH	2.573	3.928	3.779
18e	$-S(C_6H_5)$	2.478	3.758	3.115
18f	$-N(CH_3)_2$	2.621	2.581	3.229



21a-21h

Compound	R_1	R_2	R_3	Predicted antioxidant activity (pIC_{50})		
				Model 1	Model 2	Model 3
21a	$-C_6H_5$	-H	$-OCH_3$	3.967	3.831	3.549
21b	$-C_6H_5$	$-OCH_3$	$-OCH_3$	4.389	2.952	4.174
21c	$-C_6H_5$	$-N(CH_3)_2$	$-OCH_3$	3.734	2.746	3.737
21d	$-C_6H_5$	-OH	$-OCH_3$	4.258	3.885	5.634
21e	$-C_6H_5$	$-NH_2$	$-OCH_3$	3.799	3.903	5.258
21f	$-C_6H_5$	-H	$-NH_2$	3.742	4.098	3.602
21g	$-C_6H_5$	-H	$-N(CH_3)_2$	3.918	3.745	3.584
21h	$-C_6H_5$	-H	-OH	3.596	4.150	3.579

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Supplementary Table 5: Values of significant molecular descriptors of 69 modified compounds in model 1

Compound	nArNHR	ISH	B04[O-O]	G2p
2a	1	0.890	0	0.1640
2b	1	0.879	0	0.1820
2c	1	0.909	0	0.1700
2d	1	0.849	0	0.1620
2e	1	0.876	0	0.1730
2f	1	0.849	0	0.1620
2g	1	0.927	0	0.1930
2h	1	0.873	0	0.1610
3a	1	0.890	0	0.1730
3b	1	0.862	0	0.1640
3c	1	0.890	0	0.1750
3d	1	0.877	0	0.1770
3e	1	0.916	0	0.1630
3f	1	0.885	1	0.1630
3g	1	0.822	1	0.1670
3h	1	0.923	0	0.1620
3i	1	0.860	0	0.1740
3j	1	0.885	0	0.1790
3k	1	0.876	0	0.1650
3l	1	0.923	1	0.1860
3m	1	0.945	1	0.1600
3n	1	0.916	0	0.1770
3o	1	0.873	0	0.1560
3p	1	0.830	1	0.1800
4a	1	0.855	1	0.1730
4b	1	0.925	1	0.1800
4c	1	0.841	0	0.1830
4d	1	0.896	0	0.1530
4e	1	0.873	1	0.1850
4f	1	0.914	1	0.1690
4g	1	0.841	0	0.1960
4h	1	0.918	0	0.1530
4i	1	0.901	1	0.1740
5a	1	0.846	1	0.1600
5b	1	0.870	0	0.1700
5c	1	0.870	0	0.1790
5d	1	0.942	1	0.1600
5e	1	0.896	1	0.1600
5f	1	0.891	1	0.1730
5g	1	0.877	1	0.1770
5h	1	0.916	1	0.1610
5i	1	0.907	1	0.1560
5j	1	0.914	1	0.1560
5k	1	0.797	0	0.1630
5l	1	0.896	0	0.1760

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Supplementary Table 5 (cont.): Values of significant molecular descriptors of 69 modified compounds in model 1

Compound	nArNHR	ISH	B04[O-O]	G2p
11a	1	0.904	0	0.1610
11b	1	0.877	1	0.1600
11c	1	0.955	0	0.1660
11d	1	0.881	1	0.1760
11e	1	0.884	0	0.1580
11f	1	0.896	1	0.1560
13a	1	0.927	0	0.1510
13b	1	0.913	1	0.1730
13c	1	0.896	1	0.1690
13d	1	0.895	1	0.1600
18a	0	0.911	1	0.1900
18b	0	0.840	1	0.2150
18c	0	0.831	0	0.1940
18d	0	0.905	0	0.1880
18e	0	0.895	0	0.1710
18f	0	0.858	0	0.1690
21a	1	0.847	0	0.1780
21b	1	0.831	1	0.1730
21c	1	0.867	0	0.1600
21d	1	0.869	1	0.1770
21e	1	0.901	0	0.1860
21f	1	0.884	0	0.1700
21g	1	0.811	0	0.1530
21h	1	0.931	0	0.1770

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Supplementary Table 6: Values of significant molecular descriptors of 69 modified compounds in model 2

Compound	D491	D467	D278	D384	D580	D461
2a	0.611	0.694	0.489	0	5.412	0.497
2b	0.630	0.636	0.505	0	5.424	0.628
2c	0.614	0.663	0.496	0	5.423	0.548
2d	0.661	0.638	0.520	0	5.448	0.427
2e	0.686	0.593	0.532	0	5.451	0.556
2f	0.640	0.649	0.520	4	5.447	0.425
2g	0.616	0.664	0.525	4	5.424	0.422
2h	0.701	0.601	0.528	4	5.446	0.325
3a	0.521	0.743	0.489	7	5.418	0.493
3b	0.507	0.754	0.489	0	5.425	0.548
3c	0.624	0.666	0.505	0	5.445	0.301
3d	0.563	0.713	0.496	0	5.445	0.395
3e	0.537	0.730	0.500	0	5.421	0.393
3f	0.499	0.757	0.531	0	5.433	0.207
3g	0.648	0.582	0.486	0	5.439	0.193
3h	0.476	0.758	0.523	0	5.428	0.189
3i	0.702	0.512	0.474	0	5.435	0.181
3j	0.501	0.734	0.531	0	5.427	0.229
3k	0.387	0.757	0.433	0	5.431	0.302
3l	0.544	0.693	0.531	0	5.459	0.547
3m	0.869	0.751	0.486	0	5.469	0.525
3n	0.535	0.736	0.523	0	5.448	0.551
3o	0.945	0.795	0.474	0	5.463	0.526
3p	0.829	0.645	0.475	0	5.487	0.345
4a	0.505	0.799	0.501	0	5.462	0.178
4b	0.602	0.773	0.454	0	5.469	0.173
4c	0.490	0.795	0.495	0	5.456	0.168
4d	0.635	0.769	0.446	0	5.465	0.167
4e	0.582	0.684	0.501	0	5.479	0.418
4f	0.796	0.739	0.454	0	5.488	0.646
4g	0.608	0.696	0.495	0	5.469	0.435
4h	0.872	0.772	0.446	0	5.482	0.770
4i	0.759	0.736	0.443	0	5.510	0.464
5a	0.632	0.627	0.462	0	5.424	0.183
5b	0.454	0.803	0.498	0	5.416	0.172
5c	0.475	0.782	0.506	0	5.415	0.205
5d	0.644	0.674	0.495	0	5.446	0.357
5e	0.454	0.804	0.440	0	5.472	0.409
5f	0.749	0.868	0.501	0	5.472	0.493
5g	0.471	0.746	0.526	0	5.461	0.297
5h	0.497	0.742	0.538	0	5.451	0.340
5i	0.837	0.909	0.489	0	5.465	0.595
5j	0.687	0.793	0.441	0	5.348	0.470
5k	0.696	0.549	0.451	0	5.421	0.176
5l	0.365	0.806	0.410	0	5.418	0.286

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Supplementary Table 6 (cont.): Values of significant molecular descriptors of 69 modified compounds in model 1

Compound	D491	D467	D278	D384	D580	D461
11a	0.324	0.690	0.489	0	5.539	0.022
11b	0.669	0.796	0.495	0	5.539	0.207
11c	0.325	0.823	0.425	0	5.539	0.313
11d	0.260	0.811	0.432	0	5.539	0.310
11e	0.466	0.590	0.481	0	5.539	0.244
11f	0.988	0.722	0.490	0	5.539	0.396
13a	0.414	0.533	0.452	0	5.586	0.349
13b	0.405	0.603	0.492	0	5.586	0.419
13c	0.577	0.716	0.456	0	5.586	0.439
13d	0.799	0.640	0.458	0	5.586	0.455
18a	0.669	0.385	0.433	0	5.442	0.284
18b	0.401	0.560	0.465	0	5.439	0.367
18c	0.377	0.595	0.473	0	5.436	0.299
18d	0.413	0.558	0.465	0	5.435	0.422
18e	0.288	0.704	0.371	0	5.438	0.498
18f	0.747	0.355	0.431	0	5.440	0.239
21a	0.344	0.709	0.380	0	5.412	0.308
21b	0.566	0.638	0.386	0	5.454	0.577
21c	0.645	0.654	0.387	0	5.448	0.650
21d	0.350	0.657	0.419	0	5.445	0.436
21e	0.350	0.689	0.416	0	5.437	0.481
21f	0.304	0.822	0.399	0	5.412	0.579
21g	0.352	0.627	0.381	0	5.412	0.216
21h	0.316	0.857	0.403	0	5.412	0.570

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Supplementary Table 7: Values of significant molecular descriptors of 69 modified compounds in model 3

Compound	SHBint4	SpMin2_Bhe	MATS8e	SssCH2
2a	4.801	1.814	0.404	0
2b	5.150	1.847	-0.295	0
2c	4.872	1.839	-0.104	0
2d	5.130	1.814	0.425	0
2e	5.480	1.847	-0.205	0
2f	4.415	1.818	0.424	0
2g	4.211	1.818	0.400	0
2h	4.572	1.818	0.490	0
3a	4.211	1.813	-0.303	0
3b	4.567	1.813	-0.325	0
3c	4.804	1.813	0.419	0
3d	4.649	1.813	0.268	0
3e	4.449	1.813	0.053	0
3f	7.165	1.813	-0.057	0
3g	4.280	1.813	-0.134	0
3h	6.953	1.813	-0.143	0
3i	4.123	1.813	-0.291	0
3j	6.731	1.813	-0.198	0
3k	4.023	1.814	-0.226	0
3l	7.304	1.813	-0.314	0
3m	5.772	1.813	-0.216	0
3n	13.064	1.813	-0.281	0
3o	4.266	1.813	-0.179	0
3p	5.862	1.813	-0.334	0
4a	7.529	1.813	-0.127	0
4b	4.498	1.813	-0.177	0
4c	7.432	1.813	-0.197	0
4d	4.341	1.813	-0.293	0
4e	7.661	1.813	-0.291	0
4f	6.041	1.813	-0.216	0
4g	13.660	1.813	-0.228	0
4h	4.491	1.813	-0.170	0
4i	6.133	1.813	-0.303	0
5a	4.393	1.813	-0.019	0
5b	7.213	1.813	0.004	0
5c	6.807	1.813	-0.050	0
5d	7.234	1.813	0.120	0
5e	6.914	1.813	-0.010	0
5f	9.160	1.813	-0.090	0
5g	10.790	1.813	-0.001	0
5h	16.903	1.813	0.063	0
5i	7.532	1.813	-0.143	0
5j	1.295	1.813	-0.097	0
5k	4.239	1.813	-0.192	0
5l	4.145	1.814	-0.100	0

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Supplementary Table 7 (cont.): Values of significant molecular descriptors of 69 modified compounds in model 1

Compound	SHBint4	SpMin2_Bhe	MATS8e	SssCH2
11a	2.048	1.884	-0.058	0
11b	2.106	1.874	-0.163	0
11c	2.058	1.911	-0.125	0
11d	2.112	1.882	-0.117	0
11e	1.974	1.893	-0.003	0
11f	4.384	1.875	-0.158	0
13a	1.965	1.899	-0.008	0
13b	2.017	1.888	-0.020	-0.261
13c	2.025	1.891	-0.063	0
13d	4.368	1.879	-0.125	0
18a	0.000	1.859	-0.102	0
18b	3.212	1.859	0.011	0
18c	2.894	1.859	-0.100	0
18d	2.542	1.859	-0.175	0
18e	0.000	1.859	-0.182	0
18f	0.000	1.859	-0.298	0
21a	2.060	1.843	-0.181	0
21b	4.287	1.843	-0.219	0
21c	2.679	1.843	-0.203	0
21d	9.823	1.843	-0.219	0
21e	8.619	1.843	-0.158	0
21f	2.033	1.849	-0.203	0
21g	1.939	1.859	-0.137	0
21h	2.100	1.840	-0.220	0