Supplementary Material

Title:

Integrating Computational Modeling and Experimental Validation to Unveil Tyrosinase Inhibition Mechanisms of Flavonoids from *Alhagi graecorum*

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Content

Cartesian coordinates of DFT optimized flavonoids at the B3LYP level of theory.

Compound **1**

C	0.56751	3.56298	0.34468
C	0.97179	2.22614	0.35112
C	2.33967	1.97828	0.2584
C	3.29344	3.00988	0.14971
C	2.85188	4.36216	0.13428
C	1.49105	4.62691	0.24402
C	4.70226	2.7053	0.06055
C	5.04373	1.28828	0.08049
C	4.07112	0.32919	0.19403
C	4.28559	-1.12941	0.22449
C	5.46375	-1.67851	0.75161
C	3.28977	-1.99468	-0.27663
C	5.6604	-3.06057	0.76981
H	6.23096	-1.02701	1.14675
C	3.49241	-3.36726	-0.27243
H	2.36139	-1.60414	-0.67711
C	4.68357	-3.90654	0.25557
H	6.57718	-3.4622	1.18697
O	2.75063	0.66907	0.28366
O	5.57839	3.60042	-0.03436
O	2.54847	-4.21287	-0.78434
H	2.90987	-5.11295	-0.69762
O	4.74556	-5.27594	0.19377
O	6.36189	0.92023	0.04341
O	3.73296	5.37256	0.02339
H	0.23201	1.43597	0.43302

O	-0.74612	3.86874	0.43064
H	-0.79241	4.84277	0.36158
H	4.63444	4.93961	-0.0231
H	1.14293	5.63866	0.25222
H	5.66419	-5.55444	0.1812
C	7.1851	2.08362	0.16064
C	7.36946	3.06611	1.11142
O	8.01902	2.31389	-0.9344
C	8.37523	3.96661	0.58765
C	8.73899	3.47447	-0.64889
H	9.78539	3.25101	-0.64751
C	8.44532	4.53486	-1.72636
H	7.9362	5.36408	-1.28129
H	7.83001	4.10664	-2.48986
O	9.67535	4.98357	-2.30131
H	9.51178	5.75901	-2.8431
H	7.96834	4.95091	0.48521
H	7.70937	2.63019	2.02757
H	6.37802	2.65647	-0.246
O	9.5099	3.99302	1.45754
H	9.74352	4.90364	1.65195
O	6.14539	3.77258	1.32922
H	6.20593	4.27453	2.1453

Compound **2**

C	0.56751	3.56298	0.34468
C	0.97179	2.22614	0.35112
C	2.33967	1.97828	0.2584
C	3.29344	3.00988	0.14971

C	2.85188	4.36216	0.13428
C	1.49105	4.62691	0.24402
C	4.70226	2.7053	0.06055
C	5.04373	1.28828	0.08049
C	4.07112	0.32919	0.19403
C	4.28559	-1.12941	0.22449
C	5.46375	-1.67851	0.75161
C	3.28977	-1.99468	-0.27663
C	5.6604	-3.06057	0.76981
H	6.23096	-1.02701	1.14675
C	3.49241	-3.36726	-0.27243
H	2.36139	-1.60414	-0.67711
C	4.68357	-3.90654	0.25557
H	6.57718	-3.4622	1.18697
O	2.75063	0.66907	0.28366
O	5.57839	3.60042	-0.03436
O	2.54847	-4.21287	-0.78434
H	2.90987	-5.11295	-0.69762
O	4.74556	-5.27594	0.19377
O	6.36189	0.92023	0.04341
O	3.73296	5.37256	0.02339
H	0.23201	1.43597	0.43302
O	-0.74612	3.86874	0.43064
H	-0.79241	4.84277	0.36158
H	4.63444	4.93961	-0.0231
H	1.14293	5.63866	0.25222
H	5.66419	-5.55444	0.1812
C	7.1851	2.08362	0.16064

C	8.05663	2.21558	-1.07207
H	6.50472	2.97244	0.23314
C	8.97356	3.16213	1.53978
C	9.00531	3.39073	-0.95113
H	7.40925	2.3472	-1.97762
C	9.84401	3.2961	0.30708
H	8.38319	4.10509	1.68349
H	8.41584	4.34505	-0.93493
H	10.52659	2.40888	0.23447
O	8.02432	1.98749	1.41851
O	10.66464	4.46128	0.42455
H	11.55674	4.25537	0.13584
O	9.86182	3.43428	-2.09542
H	9.93631	4.3397	-2.40567
O	8.80947	1.0133	-1.25276
H	9.10457	0.95393	-2.16435
C	9.86408	2.97973	2.78289
H	10.62119	2.25258	2.57568
H	9.26531	2.64691	3.60484
O	10.47937	4.22697	3.11563
H	10.97901	4.13073	3.92969

Compound **3**

C	0.56751	3.56298	0.34468
C	0.97179	2.22614	0.35112
C	2.33967	1.97828	0.2584
C	3.29344	3.00988	0.14971
C	2.85188	4.36216	0.13428
C	1.49105	4.62691	0.24402

C	4.70226	2.7053	0.06055
C	5.04373	1.28828	0.08049
C	4.07112	0.32919	0.19403
C	4.28559	-1.12941	0.22449
C	5.46375	-1.67851	0.75161
C	3.28977	-1.99468	-0.27663
C	5.6604	-3.06057	0.76981
H	6.23096	-1.02701	1.14675
C	3.49241	-3.36726	-0.27243
H	2.36139	-1.60414	-0.67711
C	4.68357	-3.90654	0.25557
H	6.57718	-3.4622	1.18697
O	2.75063	0.66907	0.28366
O	5.57839	3.60042	-0.03436
O	2.54847	-4.21287	-0.78434
O	4.74556	-5.27594	0.19377
O	6.36189	0.92023	0.04341
O	3.73296	5.37256	0.02339
H	0.23201	1.43597	0.43302
O	-0.74612	3.86874	0.43064
H	-0.79241	4.84277	0.36158
H	4.63444	4.93961	-0.0231
H	1.14293	5.63866	0.25222
H	5.66419	-5.55444	0.1812
C	7.1851	2.08362	0.16064
C	7.36946	3.06611	1.11142
O	8.01902	2.31389	-0.9344
C	8.37523	3.96661	0.58765

C	8.73899	3.47447	-0.64889
H	9.78539	3.25101	-0.64751
C	8.44532	4.53486	-1.72636
H	7.9362	5.36408	-1.28129
H	7.83001	4.10664	-2.48986
O	9.67535	4.98357	-2.30131
H	9.51178	5.75901	-2.8431
H	7.96834	4.95091	0.48521
H	7.70937	2.63019	2.02757
H	6.37802	2.65647	-0.246
O	9.5099	3.99302	1.45754
H	9.74352	4.90364	1.65195
O	6.14539	3.77258	1.32922
H	6.20593	4.27453	2.1453
C	3.07918	-5.53462	-0.65699
H	4.00461	-5.60028	-1.19006
H	3.24679	-5.75358	0.37687
H	2.38325	-6.239	-1.06248

Compound **4**

C	0.56751	3.56298	0.34468
C	0.97179	2.22614	0.35112
C	2.33967	1.97828	0.2584
C	3.29344	3.00988	0.14971
C	2.85188	4.36216	0.13428
C	1.49105	4.62691	0.24402
C	4.70226	2.7053	0.06055
C	5.04373	1.28828	0.08049
C	4.07112	0.32919	0.19403

C	4.28559	-1.12941	0.22449
C	5.46375	-1.67851	0.75161
C	3.28977	-1.99468	-0.27663
C	5.6604	-3.06057	0.76981
H	6.23096	-1.02701	1.14675
C	3.49241	-3.36726	-0.27243
H	2.36139	-1.60414	-0.67711
C	4.68357	-3.90654	0.25557
H	6.57718	-3.4622	1.18697
O	2.75063	0.66907	0.28366
O	5.57839	3.60042	-0.03436
O	2.54847	-4.21287	-0.78434
H	2.90987	-5.11295	-0.69762
O	4.74556	-5.27594	0.19377
O	6.36189	0.92023	0.04341
O	3.73296	5.37256	0.02339
H	0.23201	1.43597	0.43302
O	-0.74612	3.86874	0.43064
H	-0.79241	4.84277	0.36158
H	4.63444	4.93961	-0.0231
H	1.14293	5.63866	0.25222
C	7.1851	2.08362	0.16064
C	8.05663	2.21558	-1.07207
H	6.50472	2.97244	0.23314
C	8.97356	3.16213	1.53978
C	9.00531	3.39073	-0.95113
H	7.40925	2.3472	-1.97762
C	9.84401	3.2961	0.30708

H	8.38319	4.10509	1.68349
H	8.41584	4.34505	-0.93493
H	10.52659	2.40888	0.23447
O	8.02432	1.98749	1.41851
O	10.66464	4.46128	0.42455
H	11.55674	4.25537	0.13584
O	9.86182	3.43428	-2.09542
H	9.93631	4.3397	-2.40567
O	8.80947	1.0133	-1.25276
H	9.10457	0.95393	-2.16435
C	9.86408	2.97973	2.78289
H	10.62119	2.25258	2.57568
H	9.26531	2.64691	3.60484
H	10.32447	3.91298	3.03186
C	6.11393	-5.69079	0.17505
H	6.56719	-5.46773	1.11829
H	6.1648	-6.74433	-0.00484
H	6.6337	-5.17073	-0.60231

Compound **5**

C	0.56751	3.56298	0.34468
C	0.97179	2.22614	0.35112
C	2.33967	1.97828	0.2584
C	3.29344	3.00988	0.14971
C	2.85188	4.36216	0.13428
C	1.49105	4.62691	0.24402
C	4.70226	2.7053	0.06055
C	5.04373	1.28828	0.08049
C	4.07112	0.32919	0.19403

C	4.28559	-1.12941	0.22449
C	5.46375	-1.67851	0.75161
C	3.28977	-1.99468	-0.27663
C	5.6604	-3.06057	0.76981
H	6.23096	-1.02701	1.14675
C	3.49241	-3.36726	-0.27243
H	2.36139	-1.60414	-0.67711
C	4.68357	-3.90654	0.25557
H	6.57718	-3.4622	1.18697
O	2.75063	0.66907	0.28366
O	5.57839	3.60042	-0.03436
O	2.54847	-4.21287	-0.78434
O	4.74556	-5.27594	0.19377
O	3.73296	5.37256	0.02339
H	0.23201	1.43597	0.43302
O	-0.74612	3.86874	0.43064
H	4.63444	4.93961	-0.0231
H	1.14293	5.63866	0.25222
H	5.66419	-5.55444	0.1812
C	3.07918	-5.53462	-0.65699
H	4.00461	-5.60028	-1.19006
H	3.24679	-5.75358	0.37687
H	2.38325	-6.239	-1.06248
H	6.06924	0.99235	0.00536
C	-0.81383	5.29356	0.32962
C	-1.63667	5.67833	-0.88308
H	0.23429	5.67313	0.20499
C	-1.8043	7.18088	-0.98216

H	-2.6465	5.19438	-0.81679
C	-1.57571	7.36791	1.50191
C	-2.39731	7.75368	0.28882
H	-0.80619	7.65534	-1.17461
H	-0.56548	7.85128	1.4366
H	-3.44641	7.37664	0.41363
O	-1.40884	5.86525	1.60071
C	-2.25946	7.89564	2.7769
H	-1.64984	7.67177	3.62729
H	-3.21468	7.42684	2.88948
O	-2.43247	9.31139	2.67387
H	-2.86888	9.63922	3.46361
O	-2.46191	9.17862	0.1874
H	-3.25816	9.43041	-0.28608
O	-2.65095	7.4965	-2.09052
H	-2.19716	8.10619	-2.677
O	-1.0023	5.18827	-2.06728
H	-1.65742	5.0808	-2.76072

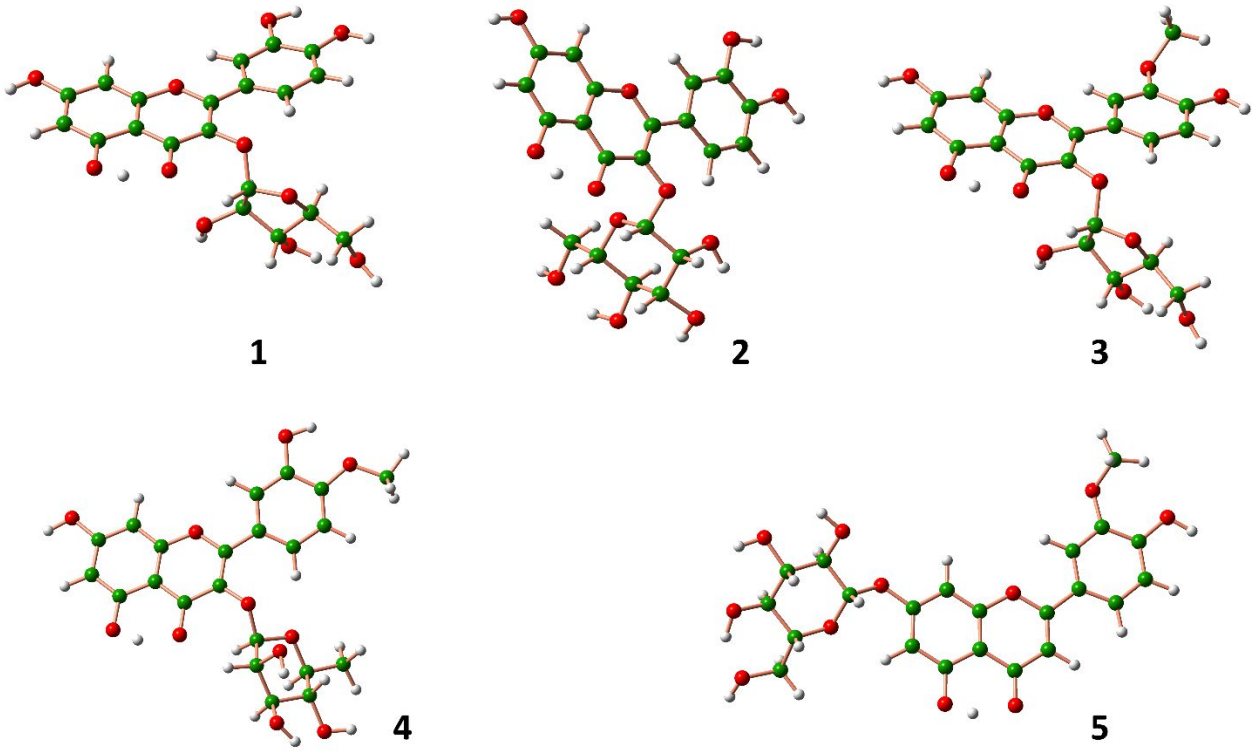

Figure S1. DFT optimized geometries of isolated flavonoids at the B3LYP level of theory.

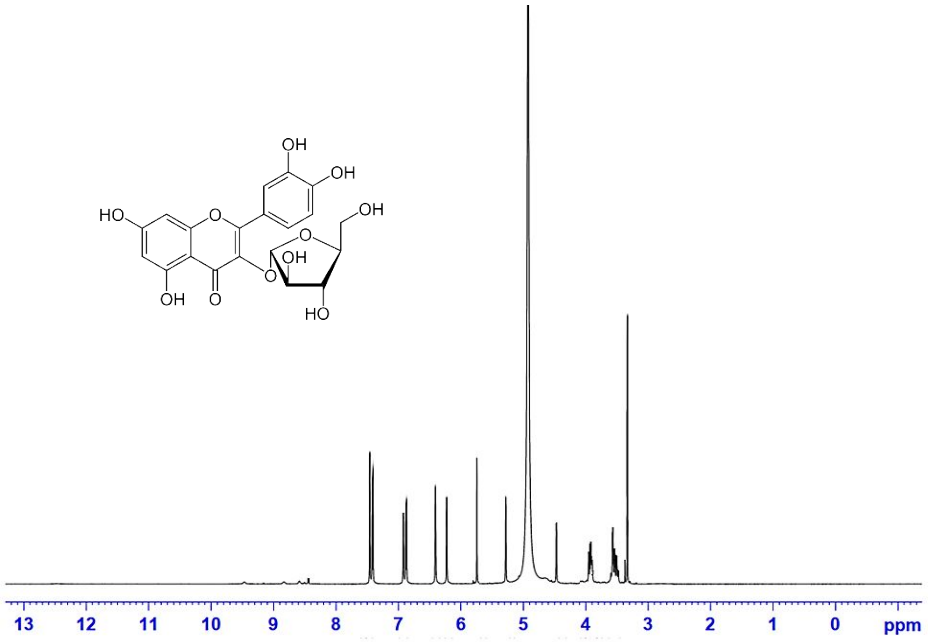

Figure S2. ^{1}H-NMR (CD_3OD-d_6) spectrum of compound **1**.

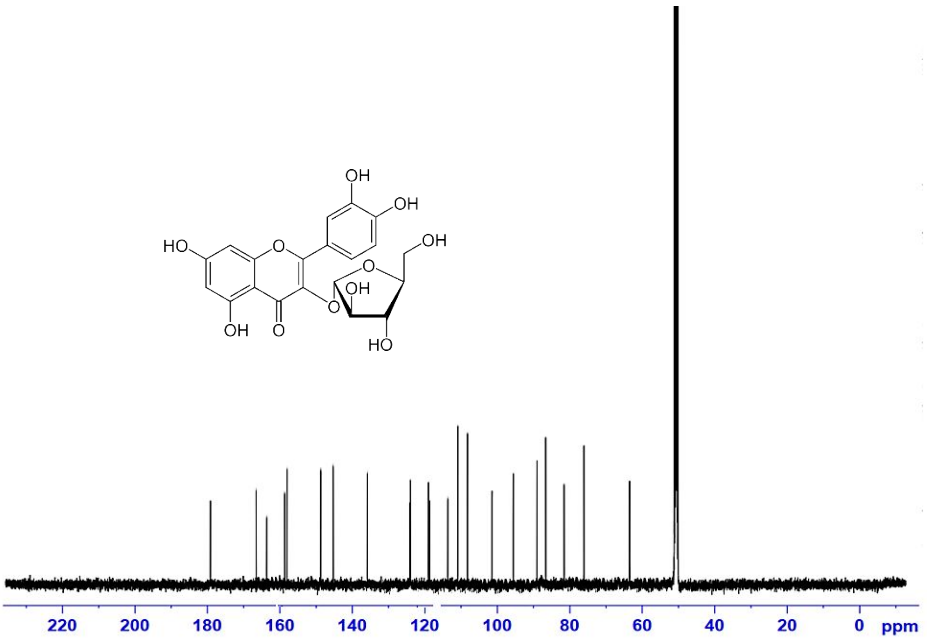

Figure S3. ^{13}C-NMR (CD_3OD-d_6)) spectrum of compound **1**.

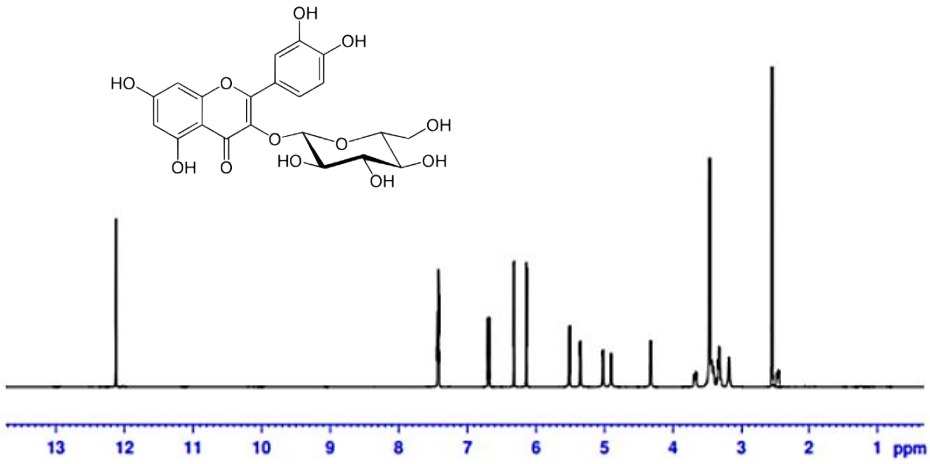

Figure S4. ^{1}H-NMR (DMSO-d_6) spectrum of compound **2**.

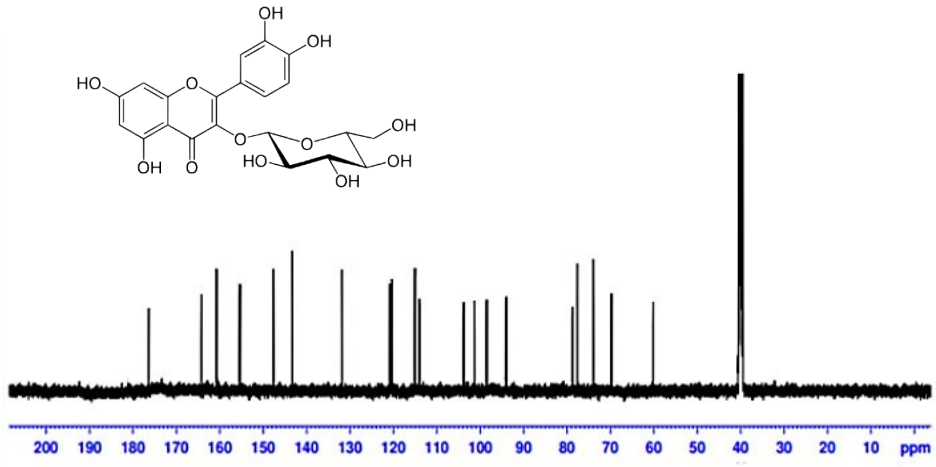

Figure S5. ^{13}C-NMR (DMSO-d_6) spectrum of compound **2**.

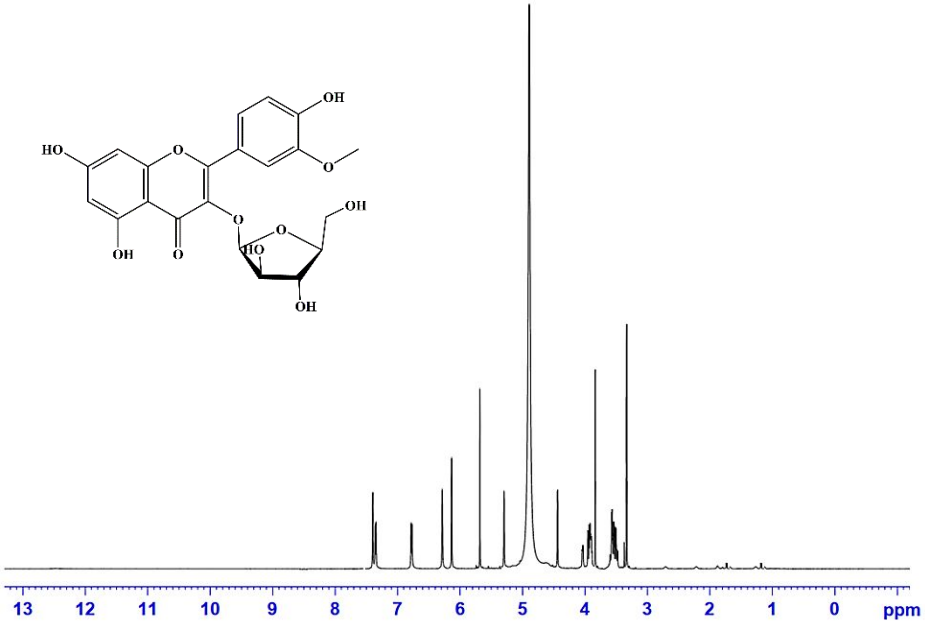

Figure S6. ^{1}H-NMR (CD_3OD-d_6) spectrum of compound **3**.

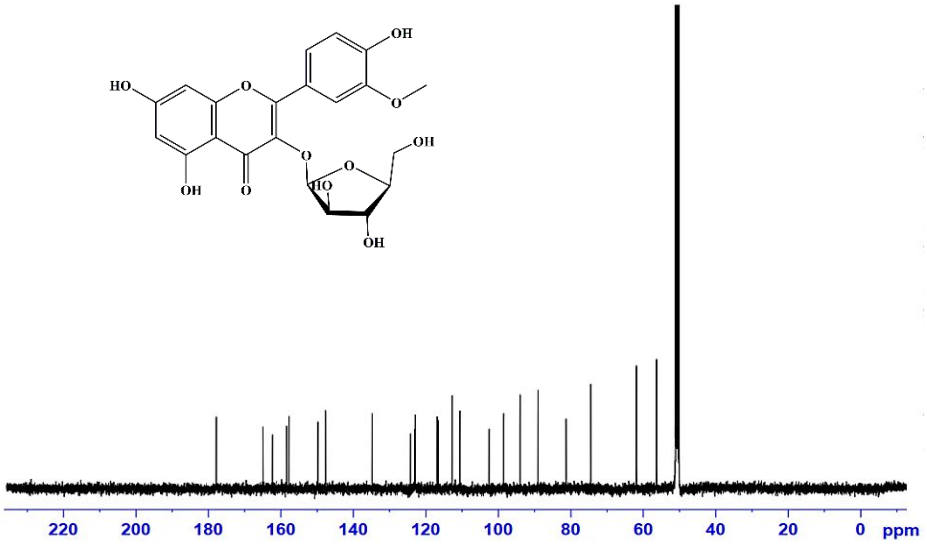

Figure S7. ^{13}C-NMR (CD_3OD-d_6) spectrum of compound **3**.

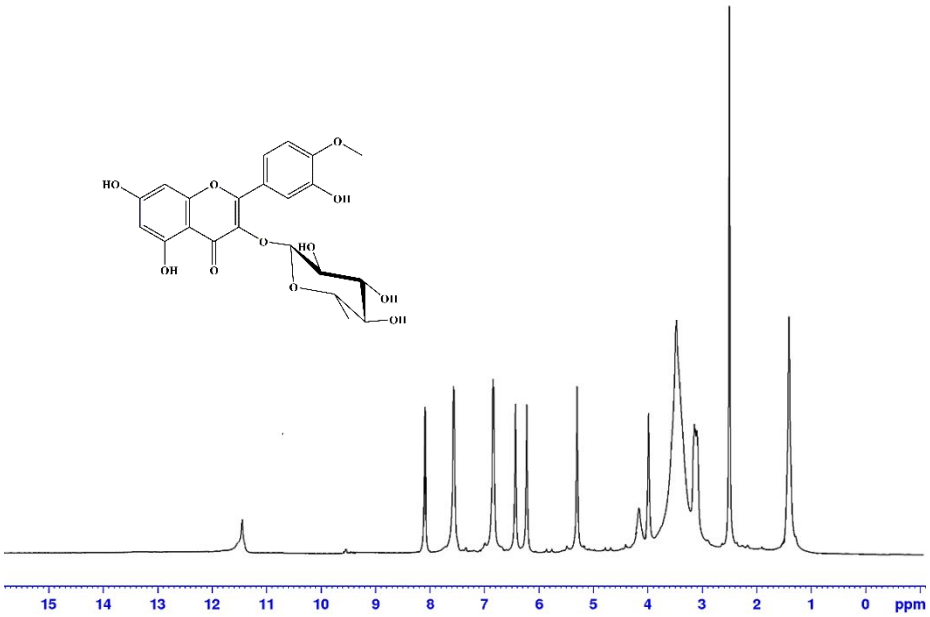

Figure S8. ^{1}H-NMR (DMSO-d_6) spectrum of compound **4**.

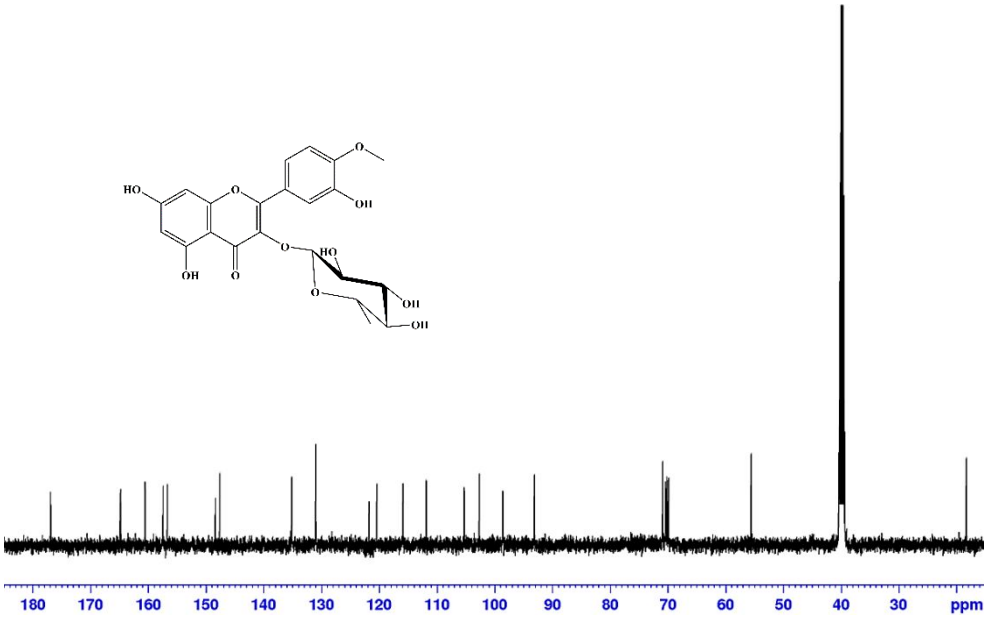

Figure S9. ^{13}C-NMR (DMSO-d_6) spectrum of compound **4**.

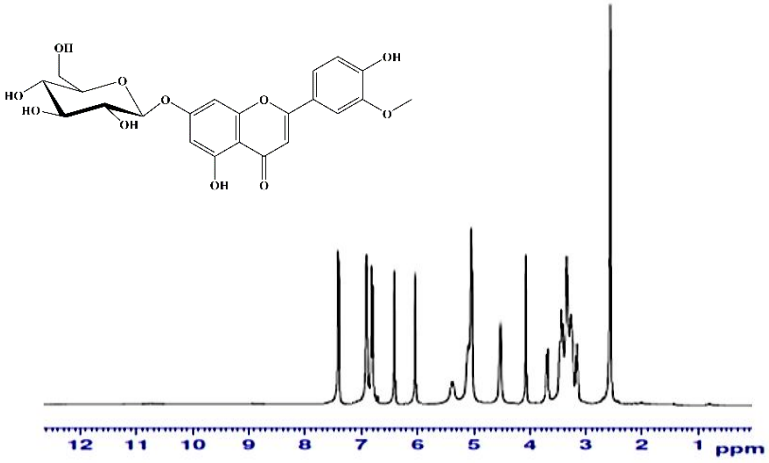

Figure S10. ^{1}H-NMR (DMSO-d_6) spectrum of compound **5**.

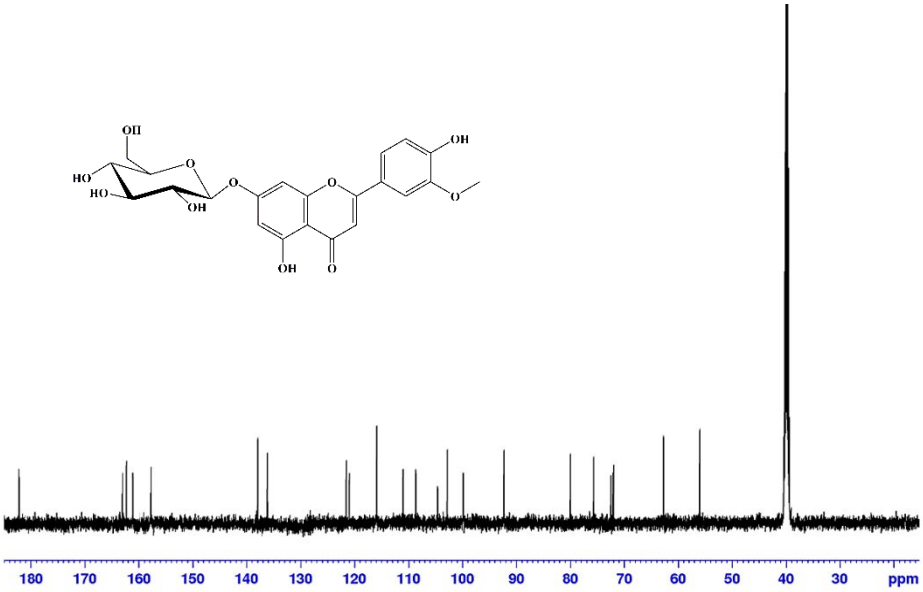

Figure S11. ^{13}C-NMR (DMSO-d_6) spectrum of compound **5**.