Supporting Information for:

Effects of hydroxyl group variations on a flavonoid backbone toward modulation of metal-free and metal-induced amyloid-β aggregation

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List of Figures and Tables

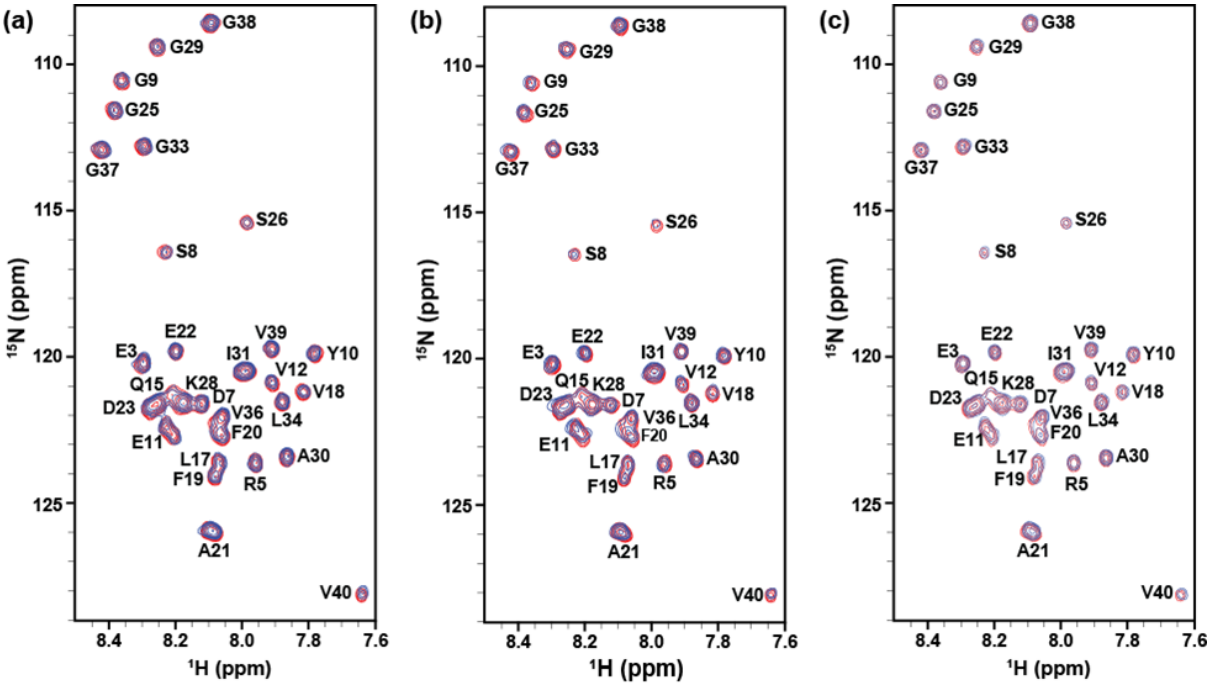

Fig. S1 Interaction of quercetin, galangin or luteolin with ^{15}N-labeled Aβ_{40}, monitored by 2D-SOFAST-HMQC NMR. Spectra were recorded as (a) quercetin, (b) galangin, or (c) luteolin was titrated into a solution of ^{15}N-labeled Aβ_{40} from 0 (red spectra) and 10 (blue spectra) equiv of flavonoids. Conditions: [Aβ_{40}] = 80 μM; [flavonoids] = 0-800 μM; 20 mM PO_4, pH 7.4, 50 mM NaCl; 7% D_2O (v/v); 10 °C.

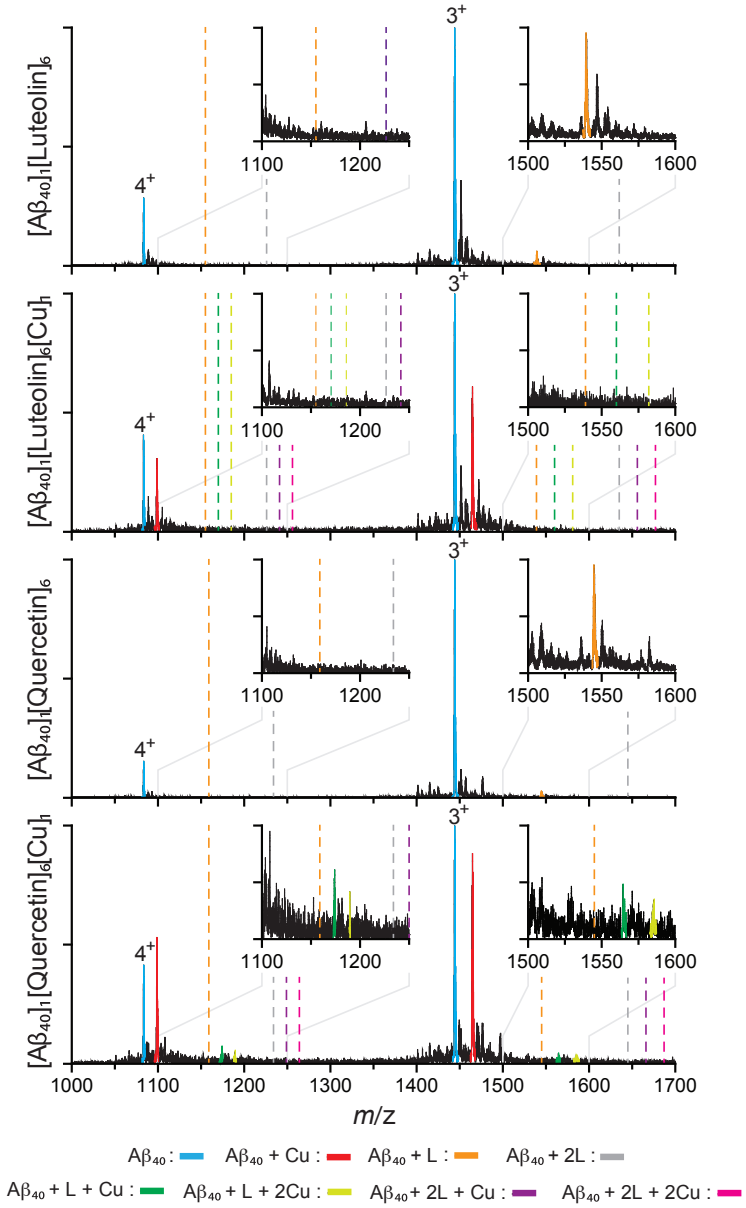

Fig. S2 Mass spectrometric analysis of luteolin- and quercetin-bound $A\beta_{40}$ monomers in both the absence and presence of Cu(II). Whilst small molecules are expected to be observed in complex with both the 3^+ and 4^+ peptide species,[1,2] luteolin and quercetin are shown to bind to only the 3^+ peptide in the absence of Cu(II).[1,2] 4^+ species binding is indicated in the samples containing a source of Cu(II). Such differences may be explained by poor binding levels of these small molecules to Aβ peptides in the absence of Cu(II). The dashed lines represent the expected binding location of the noted species based on theoretical average *m*/*z* values.

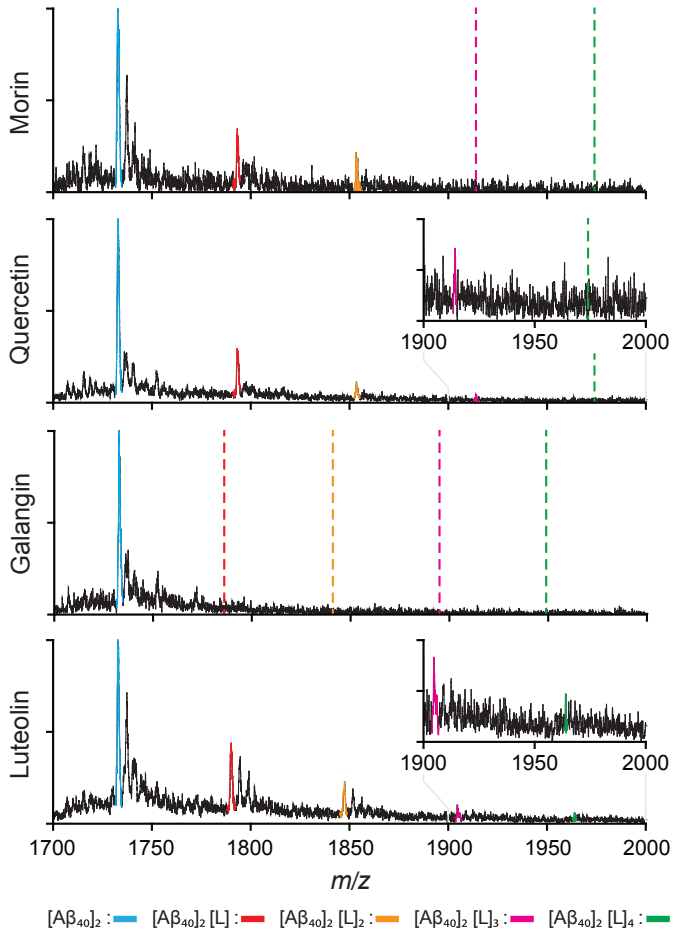

Fig. S3 Mass spectrometric analysis of flavonoid-bound $A\beta_{40}$ dimers. Mass analysis of the dimeric metal free $A\beta_{40}$ (5^{+}) in the presence of each the natural products support that whilst quercetin and luteolin are capable of binding the monomeric species, morin binds to the peptide *via* a site comprised of a surface only present in oligomeric Aβ. The dashed lines represent the expected binding location of the noted species based on theoretical average *m*/*z* values.

Table S1 K_d analysis of flavonoid-bound $A\beta_{40}$ in the absence of Cu(II).

	Dissociation Constant (μM)		
[$A\beta_{40}$][Luteolin]	9128.58	+/-	6526.54
[$A\beta_{40}$]$_2$[Luteolin]	429.99	+/-	127.48
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[$A\beta_{40}$]$_2$[Morin]	360.17	+/-	146.57
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[$A\beta_{40}$][Quercetin]	8755.75	+/-	1368.39
[$A\beta_{40}$]$_2$[Quercetin]	558.97	+/-	298.35
[$A\beta_{40}$]$_2$[Quercetin]$_2$	385.71	+/-	195.13

Values were calculated using previously published methods.[3,4] Conditions: [Aβ] = 20 μM; [Cu(II)] = 20 μM; [compound] = 120 μM. Errors shown represent single standard deviations.

Table S2 Collision cross section data of all extracted ion mobility arrival times for the observed 4^+ monomer species.

	Conformational Species (Å²)		
	1	2	3
[Aβ40]	667.33 +/- 29.05	726.42* +/- 29.05	-
[Aβ40][Cu]	669.80* +/- 27.44	735.95 +/- 27.59	801.50 +/- 31.17
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[Aβ40][Morin][Cu]	692.08* +/- 30.12	751.54 +/- 26.67	-
[Aβ40][Morin]$_2$[Cu]$_2$	693.51* +/- 27.15	770.23 +/- 28.03	811.85 +/- 30.47
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[Aβ40][Quercetin][Cu]	675.98* +/- 31.07	768.68 +/- 29.96	812.63 +/- 27.66
[Aβ40][Quercetin][Cu]$_2$	681.41* +/- 32.82	745.36 +/- 29.33	779.71 +/- 34.79

Collision Cross Section values calculated for 4^+ morin- and quercetin-bound $A\beta_{40}$ species arrival times extracted from the full width half maximum (FWHM). Errors represent least square analysis encapsulating inherent calibrant error from drift tube measurements (3%),[5] calibration curve error, and two times the replicate standard deviation error. The dominant conformational species for each extracted data set is denoted with the suffix *.

References

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