Prevention of iron- and copper-mediated DNA damage by catecholamine and amino acid neurotransmitters and comparison with L-DOPA and curcumin: metal binding as a general antioxidant mechanism

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ELECTRONIC SUPPLEMENTARY INFORMATION

DNA gel data and IC_{50} plots. Gel images of all electrophoresis results are given for experiments with epinephrine (EP), norepinephrine (NE), glycine (Gly), glutamate (Glu), 4-aminobutyrate (GABA), *l*-dihydroxyphenylalanine (L-DOPA), curcumin (Cur), and tartrate (Tart) are Fe^{2+} (Figs. S1 and S2), $Fe(EDTA)^{2-}$ (Figs. S3 and S4), Cu^{+} (Figs. S5 and S6), and $Cu(bpy)_2^{2+}$ (bpy = bipyridine; Fig. S7). In all gel electrophoresis images, damaged (nicked) plasmid DNA is in the top band; undamaged (supercoiled) DNA is in the bottom band. Tabulation of the DNA damage experimental data with dopamine (DA), EP, NE, Gly, Glu, GABA, L-DOPA, Cur, and tartrate are provided for Fe^{2+} (Tables S1-S9), $Fe(EDTA)^{2-}$ (Tables S10-S14), Cu^{+} (Tables S15-S22), and $Cu(bpy)_2^{2+}$ (bpy = bipyridine; Tables S23-S26). All data are reported as the average of at least three trials with calculated standard deviations and *p* values. Where obtained, IC_{50} plots for these compounds with Fe^{2+}, $Fe(EDTA)^{2-}$, Cu^{+}, and $Cu(bpy)_2^{2+}$ are given in Figs. S8-S10. Graphs showing correlations between IC_{50} for iron-mediated DNA damage vs. pK_a of the first phenolic hydrogen and IC_{50} and the rate of iron oxidation for the four catecholamines are provided in Fig. S11.

Electrochemical data. Cyclic voltammograms (CV) for dopamine (DA), epinephrine (EP), norepinephrine (NE), glycine (Gly), glutamate (Glu), 4-aminobutyrate (GABA), *l*-dihydroxyphenylalanine (L-DOPA), curcumin (Cur), and tartrate (Tart) at pH 6.0 with and without addition of one equiv Fe^{2+} and at pH 7.0 with and without addition of one equiv Cu^{2+} are provided in Figs. S12-S17.

UV-vis and kinetics data. UV-vis spectra are provided for the tested compounds with iron (Figs. S18, S22, and S23A) and copper (Figs. S23B and S24-S26). Initial rate plots for DA, NE, L-DOPA, and curcumin Fe^{2+} oxidation reactions with a 3:1 Fe to compound ratio are provided in Fig. S19. Absorbance vs. time graphs for all compound-to-iron ratios are given in Fig. S20, and plots of Fe^{2+} oxidation rates vs. ligand-to-iron ratios are given in Fig. S21. Table S27 lists the iron oxidation rates at all molar ratios of compound to Fe^{2+}.

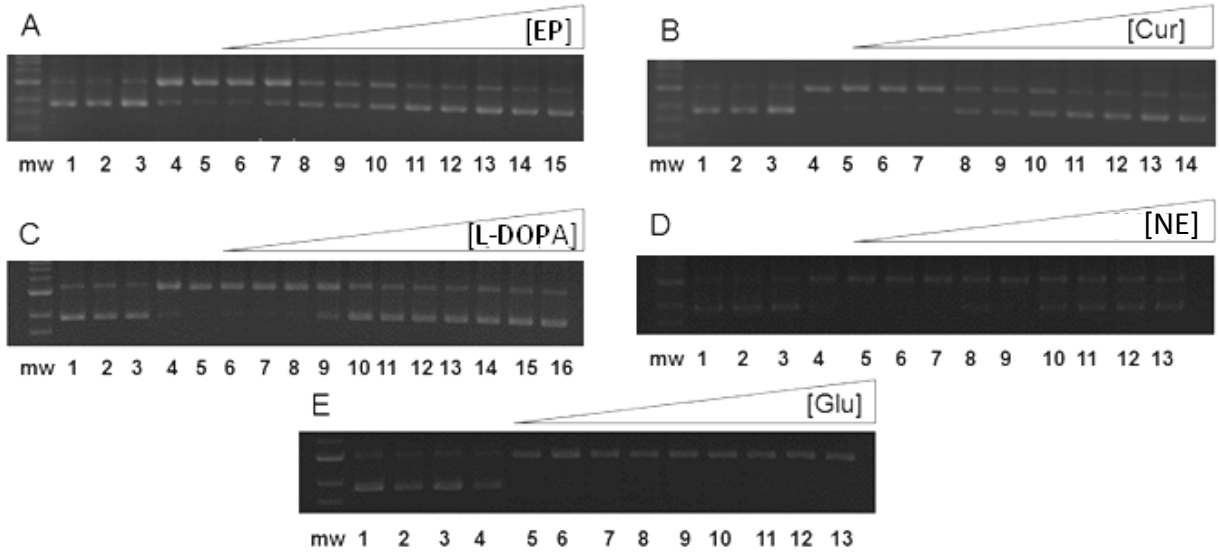

Fig. S1 Gel electrophoresis images of Fe^{2+}/H_2O_2-mediated DNA damage inhibition by A) epinephrine (EP), B) curcumin (Cur), C) *l*-dihydroxyphenylalanine (L-DOPA), D) norepinephrine (NE), and E) glutamate (Glu) in MES buffer (10 mM pH 6.0). Lanes: MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + compound (200 μM); 4 = *p* + Fe^{2+} (2 μM)/H_2O_2 (50 μM); lanes 5+ = *p* + Fe^{2+}/H_2O_2 + increasing concentrations of compound: A) 0.01, 0.1, 1, 5, 10, 25, 50, 100, 150, 200, and 300 μM EP, respectively; B) 0.01, 0.1, 1, 2, 5, 10, 25, 50, 100, and 200 μM Cur, respectively; C) 1, 2, 5, 10, 25, 50, 100, 150, 200, 250, 300, and 500 μM L-DOPA, respectively; D) 1, 2, 5, 10, 25, 50, 100, 150, and 200 μM Nor, respectively; and E) 1, 2, 5, 10, 25, 50, 100, 150, 200 μM Glu, respectively.

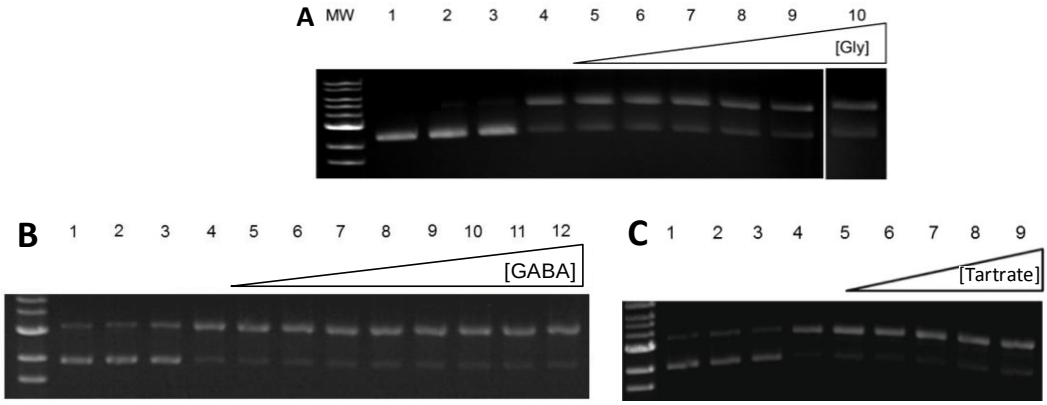

Fig. S2 Gel electrophoresis images of Fe^{2+}/H_2O_2-mediated DNA damage inhibition by A) glycine (Gly), B) 4-aminobutyrate (GABA), and C) tartrate (Tart) in MES buffer (10 mM, pH 6.0). Lanes for A) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50μM); 3 = *p* + Gly (1000 μM); 4 = *p* + Fe^{2+} (2 μM)/H_2O_2 (50 μM); 5-9 = *p* + Fe^{2+}/H_2O_2 + increasing concentrations of Gly: 1, 10, 100, 500, 1000, and 10,000 μM, respectively. Lanes for B and C) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + compound (highest concentration); 4 = *p* + Fe^{2+} (2 μM)/H_2O_2 (50 μM); lanes 5+ = *p* + Fe^{2+}/H_2O_2 + increasing concentrations of compound: B) 1, 2, 10, 25, 50, 100, 150, and 200 μM

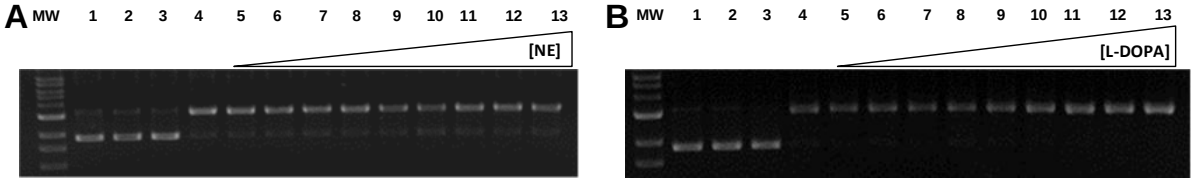

Fig. S3 Gel electrophoresis image of $Fe(EDTA)^{2-}/H_2O_2$-mediated DNA damage inhibition by A) norepinephrine (NE), and B) *l*-dihydroxyphenylalanine (L-DOPA) in MES buffer (10 mM pH 6.0). Lanes: MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 µM); 3 = *p* + compound (200 µM); 4 = *p* + $Fe(EDTA)^{2-}$ (400 µM)/H_2O_2 (50 µM); 5-13 = *p* + $Fe(EDTA)^{2-}/H_2O_2$ + increasing concentrations of compound: 1, 2, 5, 10, 25, 50, 100, 150 and 200 µM, respectively).

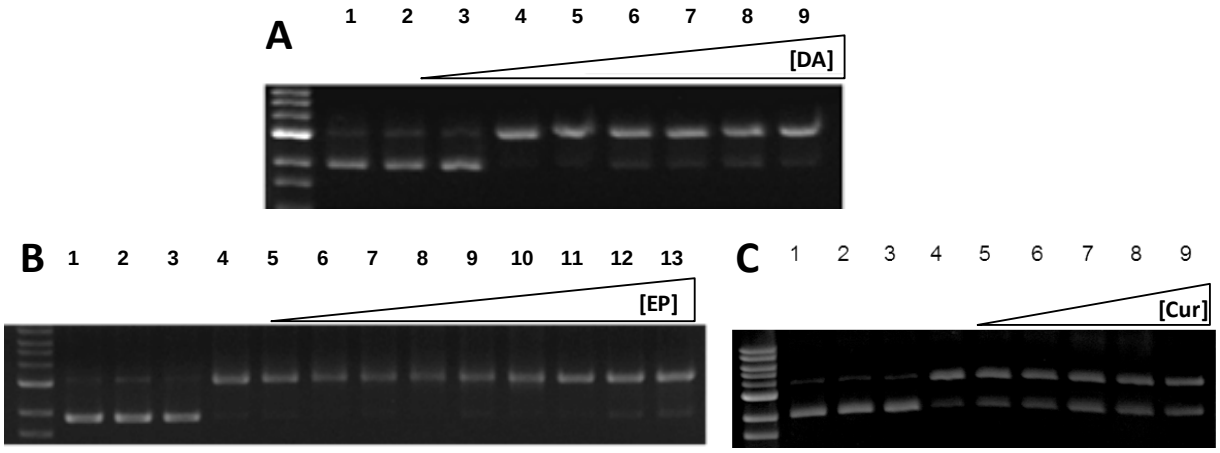

Fig. S4 Gel electrophoresis image of $Fe(EDTA)^{2-}/H_2O_2$-mediated DNA damage inhibition by A) dopamine (DA), B) epinephrine (EP), and C) curcumin (Cur) in MES buffer (10 mM pH 6.0). Lanes for A) MW = 1 kb ladder; 1 = plasmid DNA (p); 2 = p + H_2O_2; 3 = p + 1200 µM dopamine + H_2O_2; 4 = p + $Fe(EDTA)^{2-}$ + H_2O_2; lanes 5-9 = p + $Fe(EDTA)^{2-}$ + H_2O_2 + 10, 80, 600, and 1200 µM dopamine, respectively. Lanes for B) MW = 1 kb ladder; 1 = plasmid DNA (p); 2 = p + H_2O_2; 3 = p + 200 µM epinephrine + H_2O_2; 4 = p + $Fe(EDTA)^{2-}$ + H_2O_2; lanes 5-13 = p + $Fe(EDTA)^{2-}$ + H_2O_2 + 1, 2, 5, 10, 25, 50, 100, 150, and 200 µM epinephrine, respectively. Lanes for C) MW = 1 kb ladder; 1 = plasmid DNA (p); 2 = p + H_2O_2; 3 = p + 75 µM curcumin + H_2O_2; 4 = p + $Fe(EDTA)^{2-}$ + H_2O_2; lanes 5-9 = p + $Fe(EDTA)^{2-}$ + H_2O_2. + 1, 10, 25, 45, and 75 µM curcumin, respectively.

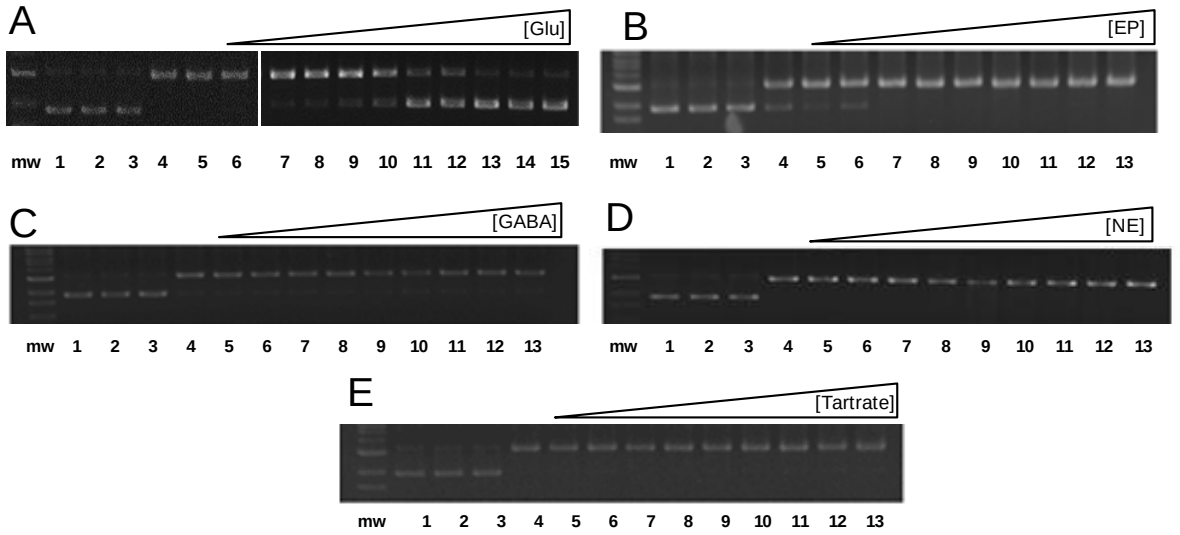

Fig. S5 Gel electrophoresis images of Cu^{+} (6 μM)/H_2O_2 (50 μM)-mediated DNA damage inhibition by A) glutamate (Glu), B) epinephrine (EP), C) 4-aminobutyrate (GABA), D) norepinephrine (NE), and E) tartrate in MOPS buffer (10 mM pH 7.0). Lanes for A) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + Glu (200 μM) + H_2O_2; 4 = *p* + Cu^{+}/H_2O_2; 5-15 = *p* + Cu^{+}/H_2O_2 + increasing concentrations of Glu: 0.3, 0.6, 1, 2, 5, 10, 25, 50, 100, 150, and 200 μM, respectively. Lanes for B-E) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + compound (200 μM) + H_2O_2; 4 = *p* + Cu^{+}/H_2O_2; 5-13 = *p* + Cu^{+}/H_2O_2 + increasing concentrations of compound: 1, 2, 5, 10, 25, 50, 100, 150, and 200 μM, respectively.

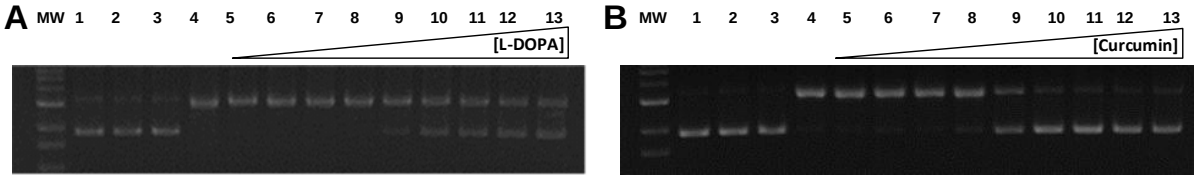

Fig. S6 Gel electrophoresis images of Cu^{+} (6 μM)/H_2O_2 (50 μM)-mediated DNA damage inhibition by A) *l*-dihydroxyphenylalanine (L-DOPA), and B) curcumin in MOPS buffer (10 mM pH 7.0). Lanes: MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + H_2O_2 + compound (200 μM); 4 = *p* + Cu^{+}/H_2O_2; 5-13 = *p* + Cu^{+}/H_2O_2 + increasing concentrations of compound: 1, 2, 5, 10, 25, 50, 100, 150, and 200 μM, respectively.

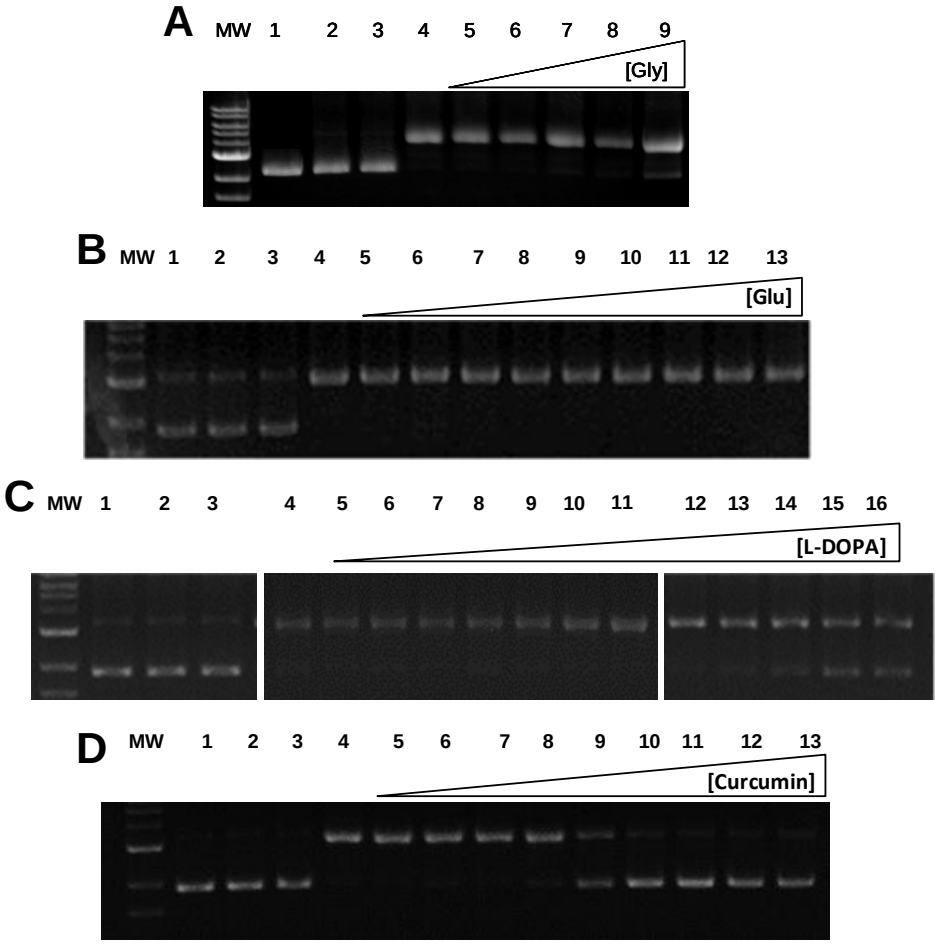

Fig. S7 Gel electrophoresis images of $Cu(bpy)^{2+}/H_2O_2$-mediated DNA damage inhibition by A) glycine (Gly), B) glutamate (Glu), C) *l*-dihydroxyphenylalanine (L-DOPA), and D) curcumin in MOPS buffer (10 mM pH 7.0). Lanes for A) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + Gly (1000 μM); 4 = *p* + $Cu(bpy)_2^+$ (400 μM)/H_2O_2 (50 μM); 5-9 = *p* + $Cu(bpy)_2^+$ /H_2O_2 (50 μM) + increasing concentrations of Gly: 1, 10, 100, 500, and 1000 μM, respectively. Lanes for B) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + Glu (200 μM); 4 = *p* + $Cu(bpy)_2^+$ (400 μM)/H_2O_2 (50 μM); 5-13 = *p* + $Cu(bpy)_2^+$ / H_2O_2 + increasing concentrations of Glu: 1, 2, 5, 10, 25, 50, 100, 150 and 200 μM, respectively. Lanes for C) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + L-DOPA (500 μM); 4 = *p* + $Cu(bpy)_2^+$ (400 μM)/H_2O_2 (50 μM); 5-13 = *p* + $Cu(bpy)_2^+$ (400 μM)/H_2O_2 (50 μM) + increasing concentrations of L-DOPA: 1, 2, 5, 10, 25, 50, 100, 150, 200, 300, 400 and 500 μM, respectively. Lanes for D) MW = 1 kb DNA ladder; 1 = plasmid DNA (*p*); 2 = *p* + H_2O_2 (50 μM); 3 = *p* + curcumin (200 μM); 4 = *p* + $Cu(bpy)_2^+$ (50 μM)/H_2O_2 (50μM); 5-13 = *p* + $Cu(bpy)_2^+$ (50 μM)/H_2O_2 (50 μM) + increasing concentrations of curcumin: 1, 2, 5, 10, 25, 50, 100, 150, 200 μM, respectively.

Table S1 Tabulation of gel electrophoresis results for dopamine (DA) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	DA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
3: p + H_2O_2 + DA	200	96.2 ± 1.2	3.8 ± 1.2	–	–
4: p + Fe^{2+} + H_2O_2	0	3.9 ± 2.3	96.1 ± 2.3	0	–
5: p + Fe^{2+} + H_2O_2 + DA	0.01	4.6 ± 2.8	95.4 ± 2.8	0.7 ± 2.1	0.841
6	0.1	7.9 ± 1.5	92.1 ± 1.5	4.2 ± 1.8	0.577
7	1	2.1 ± 3.7	97.9 ± 3.7	-1.9 ± 1.4	0.682
8	2	4.4 ± 1.2	95.6 ± 1.2	0.5 ± 2.9	0.208
9	5	12.5 ± 2.7	87.5 ± 2.7	8.9 ± 1.8	0.094
10	10	34.0 ± 3.9	66.0 ± 3.9	31.3 ± 1.2	0.052
11	25	60.8 ± 0.8	39.2 ± 0.8	59.2 ± 0.8	< 0.001
12	50	85.3 ± 2.1	14.7 ± 2.1	84.7 ± 3.5	< 0.001
13	100	90.8 ± 0.5	9.2 ± 0.5	90.4 ± 0.4	< 0.001
14	200	91.9 ± 0.7	8.1 ± 0.7	91.6 ± 1.9	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S2 Tabulation of gel electrophoresis results for epinephrine (EP) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	EP (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
3: p + H_2O_2 + EP	300	98.2 ± 1.5	1.8 ± 1.5	–	–
4: p + Fe^{2+} + H_2O_2	0	2.7 ± 0.6	97.3 ± 0.6	0	–
5: p + Fe^{2+} + H_2O_2 + EP	0.01	1.0 ± 1.5	99.0 ± 1.5	-1.7 ± 0.7	0.863
6	0.1	4.7 ± 0.9	95.3 ± 0.9	2.1 ± 0.4	0.715
7	1	17.5 ± 3.1	82.5 ± 3.1	15.2 ± 0.9	0.064
8	5	54.4 ± 2.7	45.6 ± 2.7	53.1 ± 0.4	0.001
9	10	73.6 ± 0.5	26.4 ± 0.5	72.9 ± 0.7	< 0.001
10	25	85.7 ± 2.3	14.3 ± 2.3	85.3 ± 1.0	< 0.001
11	50	97.2 ± 1.4	2.7 ± 1.4	97.1 ± 0.5	< 0.001
12	100	96.5 ± 5.9	3.5 ± 5.9	96.4 ± 0.4	< 0.001
13	200	98.2 ± 2.0	1.8 ± 2.0	98.2 ± 0.9	< 0.001
14	300	95.3 ± 3.1	4.7 ± 3.1	95.1 ± 0.3	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S3 Tabulation of gel electrophoresis results for norepinephrine (NE) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	NE (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
3: p + H_2O_2 + NE	100	98.6 ± 0.3	1.4 ± 0.3	–	–
4: p + Fe^{2+} + H_2O_2	0	7.6 ± 0.6	92.4 ± 0.6	0	–
5: p + Fe^{2+} + H_2O_2 + NE	0.2	0 ± 0.6	100.0 ± 0.6	-8.23 ± 1.2	0.001
6	0.4	0 ± 0.2	100.0 ± 0.2	-8.23 ± 1.5	0.001
7	1	3.6 ± 0.4	96.4 ± 0.4	3.6 ± 3.2	0.001
8	2	0.9 ± 0.3	99.1 ± 0.3	46.1 ± 8.4	0.001
9	5	26.5 ± 1.1	73.5 ± 1.1	65.5 ± 2.6	< 0.001
10	10	73.8 ± 0.2	16.2 ± 0.2	78.4 ± 3.6	< 0.001
11	25	79.5 ± 0.9	10.5 ± 0.9	93.7 ± 11.4	< 0.001
12	50	82.5 ± 2.0	17.5 ± 2.0	96.2 ± 0.3	< 0.001
13	100	87.2 ± 0.0	12.8 ± 0.0	107.8 ± 0.9	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S4 Tabulation of gel electrophoresis results for glycine (Gly) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	Gly (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	100 ± 0	100 ± 0	–	–
2: p + H_2O_2	0	100 ± 0	100 ± 0	–	–
3: p + Gly	1000	99.7 ± 0.54	0.32 ± 0.54	–	–
4: p + Fe^{2+} + H_2O_2	0	19.0 ± 3.4	81.0	0.0	–
5: p + Fe^{2+} + H_2O_2 + Gly	1	24.5 ± 3.5	75.5	6.8 ± 1.9	0.03
6	10	22.5 ± 6.5	77.5	4.5 ± 4.3	0.21
7	100	24.6 ± 2.1	75.4	6.9 ± 2.9	0.05
8	500	25.3 ± 1.1	74.7	7.6 ± 4.8	0.11
9	1000	27.5 ± 6.3	72.5	10.7 ± 4.0	0.04
10	10000	41.4 ± 3.0	58.6	31.9 ± 2.2	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S5 Tabulation of gel electrophoresis results for glutamate (Glu) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	Glu (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	98.4 ± 1.7	1.6 ± 1.7	–	–
2: p + H_2O_2	0	96.0 ± 2.9	4.0 ± 2.9	–	–
3: p + H_2O_2 + Glu	200	99.5 ± 0.7	0.5 ± 0.7	–	–
4: p + Fe^{2+} + H_2O_2	0	0.0 ± 0.0	100 ± 0.0	0	–
5: p + Fe^{2+} + H_2O_2 + Glu	1	0.0 ± 0.0	100 ± 0.0	0 ± 0.0	0.265
6	2	1.7 ± 3.0	98.3 ± 3.0	1.8 ± 3.0	0.642
7	5	2.6 ± 4.4	97.4 ± 4.4	2.6 ± 4.4	0.496
8	10	0.8 ± 1.5	99.2 ± 1.5	0.9 ± 1.6	0.782
9	25	0.0 ± 0.0	100.0 ± 0.0	0.0 ± 0.0	0.471
10	50	0.0 ± 0.0	100.0 ± 0.0	0.0 ± 0.0	0.859
11	100	0.1 ± 0.2	99.9 ± 0.2	0.1 ± 0.2	0.883
12	150	0.3 ± 0.5	99.7 ± 0.5	0.3 ± 0.5	0.079
13	200	0.9 ± 1.5	99.1 ± 1.5	0.9 ± 1.5	0.486

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S6 Tabulation of gel electrophoresis results for 4-aminobutyrate (GABA) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	GABA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	97.22 ± 2.71	2.78 ± 2.71	–	–
2: p + H_2O_2	0	94.77 ± 4.93	5.23 ± 4.93	–	–
3: p + H_2O_2 + GABA	300	85.49 ± 2.00	14.51 ± 2.00	–	–
4: p + Fe^{2+} + H_2O_2	0	15.05 ± 12.69	84.95 ± 12.69	0	–
5: p + Fe^{2+} + H_2O_2 + GABA	1	11.74 ± 10.06	84.95 ± 10.06	-4.78 ± 5.44	0.267
6	5	11.57 ± 9.74	88.43 ± 9.74	-5.07 ± 5.08	0.226
7	50	13.78 ± 12.52	86.22 ± 12.52	-1.75 ± 1.07	0.105
8	75	16.69 ± 16.69	83.31 ± 16.69	2.56 ± 8.10	0.639
9	100	13.92 ± 12.61	86.08 ± 12.61	-1.55 ± 1.10	0.135
10	150	11.13 ± 9.41	88.87 ± 9.41	-5.74 ± 5.07	0.189
11	200	12.68 ± 5.59	87.32 ± 5.59	-4.39 ± 9.29	0.499
12	300	12.46 ± 5.06	87.54 ± 5.06	-4.73 ± 9.81	0.492

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S7 Tabulation of gel electrophoresis results for prevention of *l*-dihydroxyphenylalanine (L-DOPA) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	L-DOPA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	96.4 ± 3.8	3.6 ± 3.8	–	–
2: p + H_2O_2	0	95.6 ± 4.6	4.4 ± 4.6	–	–
3: p + H_2O_2 + L-DOPA	200	98.6 ± 0.3	1.4 ± 0.3	–	–
4: p + Fe^{2+} + H_2O_2	0	7.6 ± 0.6	92.4 ± 0.6	0	–
5: p + Fe^{2+} + H_2O_2 + L-DOPA	0.2	0.1 ± 0.2	99.9 ± 0.2	-8.3 ± 0.5	0.582
6	0.4	1.9 ± 0.2	98.1 ± 0.2	-6.3 ± 0.4	0.266
7	1	1.2 ± 0.4	98.8 ± 0.4	-7.1 ± 1.1	0.088
8	2	0.9 ± 0.3	99.1 ± 0.3	-8.0 ± 0.5	0.742
9	5	26.5 ± 1.1	73.5 ± 1.1	20.9 ± 0.6	< 0.001
10	10	73.8 ± 0.2	26.2 ± 0.2	73.2 ± 0.7	< 0.001
11	25	79.5 ± 0.9	20.5 ± 0.9	79.4 ± 1.5	< 0.001
12	50	82.5 ± 2.0	17.5 ± 2.0	82.8 ± 2.7	< 0.001
13	100	86.7 ± 1.2	13.3 ± 1.2	87.4 ± 1.9	< 0.001
14	150	79.9 ± 0.9	20.1 ± 0.9	79.9 ± 1.5	< 0.001
15	200	86.4 ± 0.3	13.6 ± 0.3	87.1 ± 0.9	< 0.001
16	500	87.6 ± 0.8	12.4 ± 0.8	91.1 ± 5.8	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S8 Tabulation of gel electrophoresis results for curcumin (Cur) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	Cur (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
3: p + H_2O_2 + Cur	200	97.9 ± 2.7	2.1 ± 2.7	–	–
4: p + Fe^{2+} + H_2O_2	0	4.9 ± 2.0	95.1 ± 2.0	0	–
5: p + Fe^{2+} + H_2O_2 + Cur	0.01	3.3 ± 3.8	96.7 ± 3.8	3.0 ± 2.7	0.177
6	0.1	8.2 ± 1.9	91.8 ± 1.9	3.5 ± 1.5	0.037
7	1	2.9 ± 4.1	97.1 ± 4.1	-2.1 ± 0.5	0.471
8	2	9.5 ± 1.3	90.5 ± 1.3	4.8 ± 1.2	0.192
9	5	44.7 ± 0.7	55.3 ± 0.7	41.8 ± 1.8	0.002
10	10	70.4 ± 1.6	29.6 ± 1.6	68.9 ± 0.7	< 0.001
11	25	80.4 ± 3.2	19.6 ± 3.2	79.4 ± 1.3	< 0.001
12	50	92.5 ± 3.1	7.5 ± 3.1	92.1 ± 2	< 0.001
13	100	99.0 ± 1.3	1.0 ± 1.3	99.0 ± 1.8	< 0.001
14	200	97.8 ± 1.9	2.2 ± 1.9	97.7 ± 3.9	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S9 Tabulation of gel electrophoresis results for tartrate (Tart) DNA damage assays with 2 μM Fe^{2+} and 50 μM H_2O_2.[a]

Gel lane	Tartrate (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	94.25 ± 3.87	5.75 ± 3.87	–	–
2: p + H_2O_2	0	96.47 ± 2.49	3.53 ± 2.49	–	–
3: p + H_2O_2 + Tart	400	96.40 ± 1.97	3.60 ± 1.97	–	–
4: p + Fe^{2+} + H_2O_2	0	13.21 ± 7.87	86.79 ± 7.87	0	–
5: p + Fe^{2+} + H_2O_2 + Tart	1	18.73 ± 7.86	81.27 ± 7.86	7.07 ± 0.91	0.005
6	25	16.77 ± 7.55	83.23 ± 7.55	4.33 ± 2.46	0.093
7	75	19.10 ± 9.50	80.90 ± 9.50	7.57 ± 3.64	0.069
8	200	21.93 ± 8.71	78.07 ± 8.71	11.43 ± 3.50	0.030
9	400	27.11 ± 5.85	72.89 ± 5.85	18.04 ± 1.89	0.004

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S10 Tabulation of gel electrophoresis results for dopamine (DA) DNA damage assays with 400 μM $Fe(EDTA)^{2-}$ and 50 μM H_2O_2.[a]

Gel lane	DA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	93.93 ± 1.86	6.07 ± 1.86	–	–
2: p + H_2O_2	0	92.35 ± 1.81	8.82 ± 1.81	–	–
3: p + H_2O_2 + DA	1200	94.61 ± 1.17	5.39 ± 1.17	–	–
4: p + $Fe(EDTA)^{2-}$ + H_2O_2	0	2.22 ± 1.09	97.78 ± 1.09	0	–
5: p + $Fe(EDTA)^{2-}$ + H_2O_2 + DA	10	5.16 ± 4.78	94.84 ± 4.78	3.26 ± 2.91	0.192
6	80	9.07 ± 4.98	90.93 ± 4.98	7.17 ± 3.18	0.060
7	150	15.44 ± 3.27	84.56 ± 3.27	14.79 ± 1.83	0.005
8	600	21.34 ± 2.58	78.66 ± 2.58	21.50 ± 1.44	0.001
9	1200	22.30 ± 0.25	77.70 ± 0.25	21.66 ± 1.08	0.008

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S11 Tabulation of gel electrophoresis results for epinephrine (EP) DNA damage assays with 400 μM $Fe(EDTA)^{2-}$ and 50 μM H_2O_2.[a]

Gel lane	EP (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	96.4 ± 1.1	3.6 ± 1.1	-	-
2: p + H_2O_2	0	92.4 ± 1.4	7.6 ± 1.4	-	-
3: p + H_2O_2 + EP	50	97.3 ± 1.4	2.7 ± 1.4	-	-
4: p + $Fe(EDTA)^{2-}$ + H_2O_2	0	6.2 ± 8.9	93.8 ± 8.9	0	-
5: p + $Fe(EDTA)^{2-}$ + H_2O_2 + EP	1	6.3 ± 9.7	93.7 ± 9.7	0.2 ± 1.1	0.990
6	2	4.3 ± 7.4	95.7 ± 7.4	-2.4 ± 2.3	0.791
7	5	3.4 ± 5.0	96.6 ± 5.0	-3.7 ± 5.3	0.666
8	10	5.7 ± 8.9	94.3 ± 8.9	-0.6 ± 1.5	0.948
9	25	7.0 ± 7.1	93.0 ± 7.1	0.7 ± 3.1	0.909
10	50	3.4 ± 4.2	96.6 ± 4.2	-3.7 ± 6.2	0.658
11	100	4.2 ± 2.9	95.8 ± 4.2	-3.1 ± 9.6	0.749
12	150	7.5 ± 6.4	92.5 ± 6.4	0.8 ± 9.2	0.848
13	200	10.2 ± 8.9	89.8 ± 8.9	4.5 ± 5.8	0.611

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S12 Tabulation of gel electrophoresis results for norepinephrine (NE) DNA damage assays with 400 μM $Fe(EDTA)^{2-}$ and 50 μM H_2O_2.[a]

Gel lane	NE (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	96.5 ± 4.2	3.5 ± 4.2	–	–
2: p + H_2O_2	0	97.6 ± 1.1	2.4 ± 1.1	–	–
3: p + H_2O_2 + NE	200	95.4 ± 3.5	4.6 ± 3.5	–	–
4: p + $Fe(EDTA)^{2-}$ + H_2O_2	0	4.5 ± 0.1	95.5 ± 0.1	0	–
5: p + $Fe(EDTA)^{2-}$ + H_2O_2 + NE	1	10.7 ± 0.5	89.3 ± 0.5	6.6 ± 0.4	0.002
6	2	8.8 ± 2.6	91.2 ± 2.6	4.6 ± 2.8	0.103
7	5	7.9 ± 3.0	92.1 ± 3.0	3.7 ± 3.3	0.189
8	10	8.3 ± 0.9	91.7 ± 0.9	4.0 ± 1.0	0.017
9	25	6.1 ± 0.2	93.9 ± 0.2	1.7 ± 0.2	0.012
10	50	4.5 ± 0.2	95.5 ± 0.2	0 ± 0.1	> 0.999
11	100	3.2 ± 4.0	96.8 ± 4.0	-1.4 ± 4.3	0.630
12	150	3.4 ± 5.3	96.6 ± 5.3	-1.2 ± 5.7	0.749
13	200	2.7 ± 2.7	97.3 ± 2.7	-1.9 ± 2.9	0.368

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S13 Tabulation of gel electrophoresis results for *l*-dihydroxyphenylalanine (L-DOPA) DNA damage assays with 400 μM $Fe(EDTA)^{2-}$ and 50 μM H_2O_2.[a]

Gel lane	L-DOPA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	98.1 ± 1.6	1.9 ± 1.6	–	–
2: p + H_2O_2	0	98.6 ± 0.7	1.4 ± 0.7	–	–
3: p + H_2O_2 + L-DOPA	200	99.8 ± 0.1	0.2 ± 0.1	–	–
4: p + $Fe(EDTA)^{2-}$ + H_2O_2	0	3.5 ± 1.9	96.5 ± 1.9	0	–
5: p + $Fe(EDTA)^{2-}$ + H_2O_2 + L-DOPA	1	1.5 ± 1.6	98.5 ± 1.6	-2.1 ± 3.4	0.741
6	2	2.7 ± 0.9	97.3 ± 0.9	-0.9 ± 2.9	0.796
7	5	0.5 ± 0.3	99.5 ± 0.3	-3.2 ± 2.4	0.266
8	10	6.3 ± 1.1	93.7 ± 1.1	2.9 ± 2.5	0.893
9	25	1.9 ± 0.7	98.1 ± 0.7	-1.7 ± 2.8	0.168
10	50	1.5 ± 1.6	98.5 ± 1.6	-2.1 ± 3.5	0.194
11	100	1.3 ± 1.9	98.7 ± 1.9	-2.3 ± 3.7	0.851
12	150	3.4 ± 5.3	96.6 ± 5.3	-0.2 ± 7.1	0.041
13	200	2.4 ± 3.0	97.6 ± 3.0	-1.2 ± 4.6	0.277

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S14 Tabulation of gel electrophoresis results for curcumin (Cur) DNA damage assays with 400 μM $Fe(EDTA)^{2-}$ and 50 μM H_2O_2.[a]

Gel lane	Cur (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	93.49 ± 1.48	6.51 ± 1.48	–	–
2: p + H_2O_2	0	92.99 ± 3.02	7.01 ± 3.02	–	–
3: p + H_2O_2 + Cur	75	94.26 ± 1.43	5.74 ± 1.43	–	–
4: p + $Fe(EDTA)^{2-}$ + H_2O_2	0	14.50 ± 4.94	84.35 ± 4.94	0	–
5: p + $Fe(EDTA)^{2-}$ + H_2O_2 + Cur	1	29.96 ± 4.95	70.04 ± 4.95	19.41 ± 0.88	< 0.001
6	10	35.70 ± 8.24	64.30 ± 8.24	26.73 ± 5.63	0.015
7	25	43.61 ± 6.31	56.39 ± 6.31	36.59 ± 3.40	0.003
8	45	47.35 ± 7.45	52.65 ± 7.45	41.15 ± 5.31	0.006
9	75	44.79 ± 8.46	55.21 ± 8.46	38.12 ± 6.47	0.009

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S15 Tabulation of gel electrophoresis results for epinephrine (EP) DNA damage assays with 6 μM Cu^+ and 50 μM H_2O_2.[a]

Gel lane	EP (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	97.0 ± 2.5	3.0 ± 2.5	–	–
2: p + H_2O_2	0	97.0 ± 2.0	3.0 ± 2.0	–	–
3: p + H_2O_2 + EP	200	97.4 ± 2.5	2.6 ± 2.5	–	–
4: p + Cu^+ + H_2O_2	0	4.1 ± 5.1	95.9 ± 5.1	0	–
5: p + Cu^+ + H_2O_2 + EP	1	1.6 ± 1.7	98.4 ± 1.7	-2.8 ± 5.8	0.858
6	2	2.0 ± 2.5	98.0 ± 2.5	-2.3 ± 3.0	0.123
7	5	0.9 ± 0.8	99.1 ± 0.8	-3.7 ± 5.6	0.192
8	10	1.9 ± 2.3	98.1 ± 2.3	-2.5 ± 3.3	0.574
9	25	5.6 ± 5.1	94.4 ± 5.1	1.7 ± 2.7	0.152
10	50	5.2 ± 4.6	94.8 ± 4.6	1.2 ± 4.7	0.835
11	100	2.8 ± 2.7	97.2 ± 2.7	-1.5 ± 2.9	0.202
12	150	2.5 ± 2.4	97.5 ± 2.4	-1.8 ± 3.5	0.415
13	200	4.1 ± 5.0	95.9 ± 5.0	0 ± 0.3	0.252

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S16 Tabulation of gel electrophoresis results for norepinephrine (NE) DNA damage assays with 6 μM Cu^+ and 50 μM H_2O_2.[a]

Gel lane	NE (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	94.1 ± 2.1	5.9 ± 2.1	–	–
2: p + H_2O_2	0	94.8 ± 1.9	5.2 ± 1.9	–	–
3: p + H_2O_2 + NE	200	96.3 ± 1.9	3.7 ± 1.9	–	–
4: p + Cu^+ + H_2O_2	0	0 ± 0	100 ± 0	0	–
5: p + Cu^+ + H_2O_2 + NE	1	0.4 ± 0.7	99.6 ± 0.7	0.5 ± 0	0.251
6	2	0.3 ± 0.5	99.7 ± 0.5	0.3 ± 0	0.112
7	5	0.6 ± 1.0	99.4 ± 1.0	0.6 ± 0.9	0.169
8	10	0 ± 0	100 ± 0	0 ± 0	0.894
9	25	0 ± 0	100 ± 0	0 ± 0	0.802
10	50	0 ± 0	100 ± 0	0 ± 0	0.799
11	100	0 ± 0	100 ± 0	0 ± 0	0.204
12	150	0 ± 0	100 ± 0	0 ± 0	0.819
13	200	0.2 ± 0.4	99.8 ± 0.4	0.2 ± 0	0.836

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S17 Tabulation of gel electrophoresis results for glycine (Gly) DNA damage assays with 6 μM Cu^+ and 50 μM H_2O_2.[a]

Gel lane	Gly (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	94.8 ± 1.9	5.2 ± 5.6	–	–
2: p + H_2O_2	0	94.4 ± 1.4	5.6 ± 1.4	–	–
3: p + H_2O_2 + Gly	200	95.0 ± 2.9	5.0 ± 2.9	–	–
4: p + Cu^+ + H_2O_2	0	2.0 ± 3.2	98.0 ± 3.2	0	–
5: p + Cu^+ + H_2O_2 + Gly	1	0.3 ± 0.2	99.7 ± 0.2	-1.9 ± 3.5	0.455
6	2	2.2 ± 1.8	97.8 ± 1.8	0.1 ± 4.1	0.931
7	5	9.0 ± 8.8	91.0 ± 8.8	7.6 ± 6.6	0.301
8	10	10.8 ± 3.0	89.2 ± 3.0	9.5 ± 1.3	0.026
9	25	39.5 ± 9.5	60.5 ± 9.5	40.6 ± 8.0	0.014
10	50	54.4 ± 0.2	45.6 ± 0.2	56.7 ± 2.2	0.001
11	100	63.8 ± 1.7	36.2 ± 1.7	66.8 ± 2.5	< 0.001
12	150	63.9 ± 1.8	36.1 ± 1.8	67.0 ± 4.1	< 0.001
13	200	62.7 ± 4.3	37.3 ± 4.3	65.5 ± 6.9	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S18 Tabulation of gel electrophoresis results for glutamate (Glu) DNA damage assays with 6 μM Cu^+ and 50 μM H_2O_2.[a]

Gel lane	Glu (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	94.4 ± 1.0	5.6 ± 1.0	–	–
2: p + H_2O_2	0	94.1 ± 1.0	5.9 ± 1.0	–	–
3: p + H_2O_2 + Glu	200	97.6 ± 2.5	2.4 ± 2.5	–	–
4: p + Cu^+ + H_2O_2	0	4.0 ± 4.2	96.0 ± 4.2	0	–
5: p + Cu^+ + H_2O_2 + Glu	0.3	0 ± 0.01	100 ± 0.01	-4.2 ± 0.9	0.241
6	0.6	0 ± 0.01	100 ± 0.01	-4.2 ± 0.9	0.241
7	1	11.6 ± 1.7	88.4 ± 1.7	8.2 ± 2.2	0.073
8	2	16.6 ± 2.5	83.4 ± 2.5	13.8 ± 4.0	0.018
9	5	23.4 ± 3.1	76.6 ± 3.1	20.6 ± 5.4	0.004
10	10	40.5 ± 5.0	59.5 ± 5.0	38.9 ± 6.4	0.001
11	25	75.5 ± 1.6	24.5 ± 1.6	76.6 ± 1.5	< 0.001
12	50	71.2 ± 1.3	28.8 ± 1.3	72.0 ± 1.4	< 0.001
13	100	88.1 ± 3.0	11.9 ± 3.0	90.3 ± 4.2	< 0.001
14	150	87.5 ± 2.0	12.5 ± 2.0	89.6 ± 3.1	< 0.001
15	200	87.6 ± 1.4	12.4 ± 1.4	89.7 ± 2.5	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S19 Tabulation of gel electrophoresis results for 4-aminobutyrate (GABA) DNA damage assays with 6 μM Cu^{+} and 50 μM H_2O_2.[a]

Gel lane	GABA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	97.5 ± 1.5	2.5 ± 1.5	–	–
2: p + H_2O_2	0	96.6 ± 1.0	3.4 ± 1.2	–	–
3: p + H_2O_2 + GABA	200	98.8 ± 0.7	1.2 ± 0.7	–	–
4: p + Cu^{+} + H_2O_2	0	4.7 ± 2.6	95.3 ± 2.6	0	–
5: p + Cu^{+} + H_2O_2 + GABA	1	4.0 ± 2.3	96.0 ± 2.3	-0.8 ± 0.5	0.152
6	2	5.5 ± 3.1	94.5 ± 3.1	0.9 ± 1.0	0.273
7	5	7.3 ± 3.5	92.7 ± 3.5	2.8 ± 1.8	0.467
8	10	3.4 ± 2.0	96.6 ± 2.0	-1.4 ± 1.1	0.281
9	25	4.1 ± 1.7	95.9 ± 1.7	-0.7 ± 1.4	0.714
10	50	7.2 ± 4.5	92.8 ± 4.5	2.8 ± 3.0	0.462
11	100	6.2 ± 3.3	93.8 ± 3.3	1.6 ± 1.4	0.361
12	150	2.5 ± 2.0	97.5 ± 2.0	-2.4 ± 1.4	0.896
13	200	6.7 ± 3.3	93.3 ± 3.3	2.2 ± 1.7	0.538

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S20 Tabulation of gel electrophoresis results for *l*-dihydroxyphenylalanine (L-DOPA) DNA damage assays with 6 μM Cu^{+} and 50 μM H_2O_2.[a]

Gel lane	L-DOPA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	96.5 ± 2.6	3.5 ± 2.6	–	–
2: p + H_2O_2	0	94.0 ± 0.74	6.0 ± 0.74	–	–
3: p + H_2O_2 + L-DOPA	200	93.6 ± 0.9	6.4 ± 0.9	–	–
4: p + Cu^{+} + H_2O_2	0	1.9 ± 1.1	98.1 ± 1.1	0	–
5: p + Cu^{+} + H_2O_2 + L-DOPA	1	0.7 ± 0.4	99.3 ± 0.4	-1.3 ± 1.0	0.943
6	2	0.1 ± 0.1	99.9 ± 0.1	-2.0 ± 1.2	0.101
7	5	0.2 ± 0.1	99.8 ± 0.1	-1.8 ± 1.2	0.115
8	10	1.6 ± 0.5	98.4 ± 0.5	-0.3 ± 1.6	0.124
9	25	13.2 ± 2.2	86.8 ± 2.2	12.3 ± 3.0	0.005
10	50	42.4 ± 1.3	57.6 ± 1.3	44.0 ± 1.5	< 0.001
11	100	45.9 ± 1.2	54.1 ± 1.2	47.8 ± 1.4	< 0.001
12	150	57.6 ± 0.6	42.4 ± 0.6	60.6 ± 0.6	< 0.001
13	200	63.0 ± 1.3	37.0 ± 1.3	66.4 ± 1.3	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S21 Tabulation of gel electrophoresis results for curcumin (Cur) DNA damage assays with 6 μM Cu^{+} and 50 μM H_2O_2.[a]

Gel lane	Cur (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	97.6 ± 1.6	2.4 ± 1.6	–	–
2: p + H_2O_2	0	96.4 ± 1.8	3.6 ± 1.8	–	–
3: p + H_2O_2 + Cur	200	96.4 ± 1.8	3.6 ± 1.8	–	–
4: p + Cu^{+} + H_2O_2	0	3.3 ± 2.9	96.7 ± 2.9	0	–
5: p + Cu^{+} + H_2O_2 + Cur	1	3.2 ± 3.5	96.8 ± 3.5	-0.1 ± 1.2	0.972
6	2	6.5 ± 0.4	93.5 ± 0.4	3.4 ± 3.4	0.194
7	5	8.1 ± 6.2	91.9 ± 6.2	5.2 ± 5.5	0.316
8	10	11.6 ± 2.6	88.4 ± 2.6	8.9 ± 0.5	0.021
9	25	64.7 ± 1.7	35.3 ± 1.7	65.9 ± 1.1	< 0.001
10	50	88.6 ± 3.3	11.4 ± 3.3	91.6 ± 1.7	< 0.001
11	100	92.3 ± 1.3	7.7 ± 1.3	95.6 ± 1.6	< 0.001
12	150	93.8 ± 1.2	6.2 ± 1.2	97.2 ± 1.4	< 0.001
13	200	93.8 ± 3.2	6.2 ± 3.1	97.2 ± 5.2	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S22 Tabulation of gel electrophoresis results for tartrate (Tart) DNA damage assays with 6 μM Cu^{+} and 50 μM H_2O_2.[a]

Gel lane	Tartrate (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	96.78 ± 1.7	3.22 ± 1.7	-	-
2: p + H_2O_2	0	96.99 ± 2.4	3.01 ± 2.4	-	-
3: p + H_2O_2 + Tart	200	97.33 ± 2.6	2.67 ± 2.6	-	-
4: p + Cu^{+} + H_2O_2	0	1.60 ± 1.3	98.40 ± 1.3	0	-
5: p + Cu^{+}+ H_2O_2 + Tart	1	2.95 ± 3.1	97.05 ± 3.1	1.34 ± 1.9	0.541
6	2	6.60 ± 7.5	93.40 ± 7.5	5.21 ± 5.7	0.517
7	5	1.81 ± 1.6	98.19 ± 1.6	0.20 ± 0.39	0.871
8	10	2.43 ± 2.1	97.57 ± 2.1	0.82 ± 0.85	0.598
9	25	5.22 ± 4.7	94.78 ± 4.7	3.61 ± 3.7	0.316
10	30	2.05 ± 1.8	97.95 ± 1.8	0.45 ± 0.76	0.749
11	100	5.86 ± 4.5	94.14 ± 4.6	4.25 ± 3.2	0.240
12	150	2.02 ± 0.62	97.98 ± 0.62	0.41 ± 1.6	0.630
13	200	5.50 ± 0.23	94.50 ± 0.23	3.89 ± 2.4	0.076

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S23 Tabulation of gel electrophoresis results for glycine (Gly) DNA damage assays with 50 µM $Cu(bpy)_2^+$ and 50 µM H_2O_2.[a]

Gel lane	Gly (µM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	99.4 ± 0.7	0.6 ± 0.7	–	–
2: p + H_2O_2	0	98.7 ± 1.6	1.3 ± 1.6	–	–
3: p + Gly	1000	98.9 ± 2.0	1.3 ± 2.0	–	–
4: p + $Cu(bpy)_2^+$ + H_2O_2	0	2.0 ± 2.9	98.0 ± 2.9	0.0	–
5: p + $Cu(bpy)_2^+$ + H_2O_2 + Gly	1	0.7 ± 1.2	99.3 ± 1.2	-1.5 ± 2.0	0.30
6	10	0.0 ± 0.0	100 ± 0	-2.2 ± 3.2	0.40
7	100	4.7 ± 2.6	95.3 ± 2.6	2.7 ± 2.0	0.10
8	500	5.2 ± 3.8	94.8 ± 3.8	3.3 ± 1.1	0.04
9	1000	15.2 ± 2.8	84.8 ± 2.8	13.6 ± 0.5	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S24 Tabulation of gel electrophoresis results for glutamate (Glu) DNA damage assays with 50 µM $Cu(bpy)_2^+$ and 50 µM H_2O_2.[a]

Gel lanes	Glu (µM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	93.4 ± 1.9	6.6 ± 1.9	–	–
2: p + H_2O_2	0	92.4 ± 0.6	7.6 ± 0.6	–	–
3: p + H_2O_2 + Glu	200	96.5 ± 1.6	3.5 ± 1.6	–	–
4: p + $Cu(bpy)_2^+$ + H_2O_2	0	3.7 ± 6.5	96.3 ± 6.5	0	–
5: p + $Cu(bpy)_2^+$ + H_2O_2 + Glu	1	3.1 ± 5.4	96.9 ± 5.4	-0.7 ± 1.3	0.908
6	2	3.4 ± 5.8	96.6 ± 5.8	-0.4 ± 0.8	0.955
7	5	3.3 ± 5.7	96.7 ± 5.7	-0.5 ± 1.0	0.940
8	10	3.8 ± 6.6	96.2 ± 6.6	0.1 ± 0.2	0.986
9	25	3.3 ± 5.7	96.7 ± 5.7	-0.6 ± 1.0	0.940
10	50	2.7 ± 4.7	97.3 ± 4.7	-1.2 ± 2.1	0.841
11	100	4.1 ± 7.1	95.9 ± 7.1	0.5 ± 0.8	0.946
12	150	1.9 ± 3.2	98.1 ± 3.2	-2.3 ± 4.0	0.697
13	200	2.6 ± 4.5	97.4 ± 4.5	-1.4 ± 2.4	0.823

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S25 Tabulation of gel electrophoresis results for *l*-dihydroxyphenylalanine (L-DOPA) DNA damage assays with 50 μM $Cu(bpy)_2^+$ and 50 μM H_2O_2.[a]

Gel lane	L-DOPA (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	95.0± 1.7	5.0 ± 1.7	–	–
2: p + H_2O_2	0	96.3 ± 3.4	3.7 ± 3.4	–	–
3: p + H_2O_2 + L-DOPA	500	95.8 ± 1.3	4.2 ± 1.3	–	–
4: p + $Cu(bpy)_2^+$ + H_2O_2	0	0.7 ± 1.2	99.3 ± 1.2	0	–
5: p + $Cu(bpy)_2^+$ + H_2O_2 + L-DOPA	1	0.1 ± 0.2	99.9 ± 0.2	-0.6 ± 1.0	0.479
6	2	0.5 ± 0.9	99.5 ± 0.9	-0.2 ± 0.3	0.830
7	5	0.1 ± 0.2	99.9 ± 0.2	-0.6 ± 1.0	0.479
8	10	0.2 ± 0.3	99.8 ± 0.3	-0.5 ± 0.8	0.549
9	25	0.5 ± 0.9	99.5 ± 0.9	-0.2 ± 0.3	0.830
10	50	0.2 ± 0.3	99.8 ± 0.3	-0.5 ± 0.9	0.549
11	100	0.0 ± 0.1	100.0 ± 0.1	-0.7 ± 1.1	0.419
12	150	4.9 ± 1.4	95.1 ± 0.8	-8.3 ± 1.9	0.010
13	200	12.0 ± 0.8	88.0 ± 1.5	0.2 ± 1.2	0.001
14	300	26.5 ± 1.4	73.5 ± 1.4	17.4 ± 1.4	< 0.001
15	400	48.7 ± 6.3	51.3 ± 6.3	44.0 ± 8.3	0.005
16	500	49.6 ± 1.6	50.4 ± 1.6	44.9 ± 2.8	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

Table S26 Tabulation of gel electrophoresis results for curcumin (Cur) DNA damage assays with 50 μM $Cu(bpy)_2^+$ and 50 μM H_2O_2.[a]

Gel lane	Cur (μM)	% Supercoiled	% Nicked	% Damage Inhib.	*p* Value
1: plasmid (p)	0	93.7 ± 0.1	6.3 ± 0.1	–	–
2: p + H_2O_2	0	94.6 ± 0.1	5.4 ± 0.1	–	–
3: p + H_2O_2 + Cur	200	93.1 ± 0.0	6.9 ± 0.0	–	–
4: p + $Cu(bpy)_2^+$ + H_2O_2	0	1.8 ± 0.1	98.2 ± 0.1	0	–
5: p + $Cu(bpy)_2^+$ + H_2O_2 + Cur	1	3.5 ± 0.2	96.5 ± 0.2	1.8 ± 0.2	0.001
6	2	5.3 ± 0.0	94.7 ± 0.0	3.8 ± 0.1	< 0.001
7	5	3.4 ± 0.2	96.6 ± 0.2	1.7 ± 0.3	< 0.001
8	10	9.4 ± 0.3	90.6 ± 0.3	8.2 ± 0.4	< 0.001
9	25	15.4 ± 0.5	84.6 ± 0.5	14.7 ± 0.6	< 0.001
10	50	17.2 ± 0.2	82.8 ± 0.2	16.6 ± 0.2	< 0.001
11	100	86.9 ± 0.4	13.1 ± 0.4	91.7 ± 0.5	< 0.001
12	150	86.8 ± 0.1	13.2 ± 0.1	91.6 ± 0.1	< 0.001
13	200	89.9 ± 0.4	10.1 ± 0.4	95.0 ± 0.3	< 0.001

[a]All data are reported as the average of three trials; calculated standard deviations are shown.

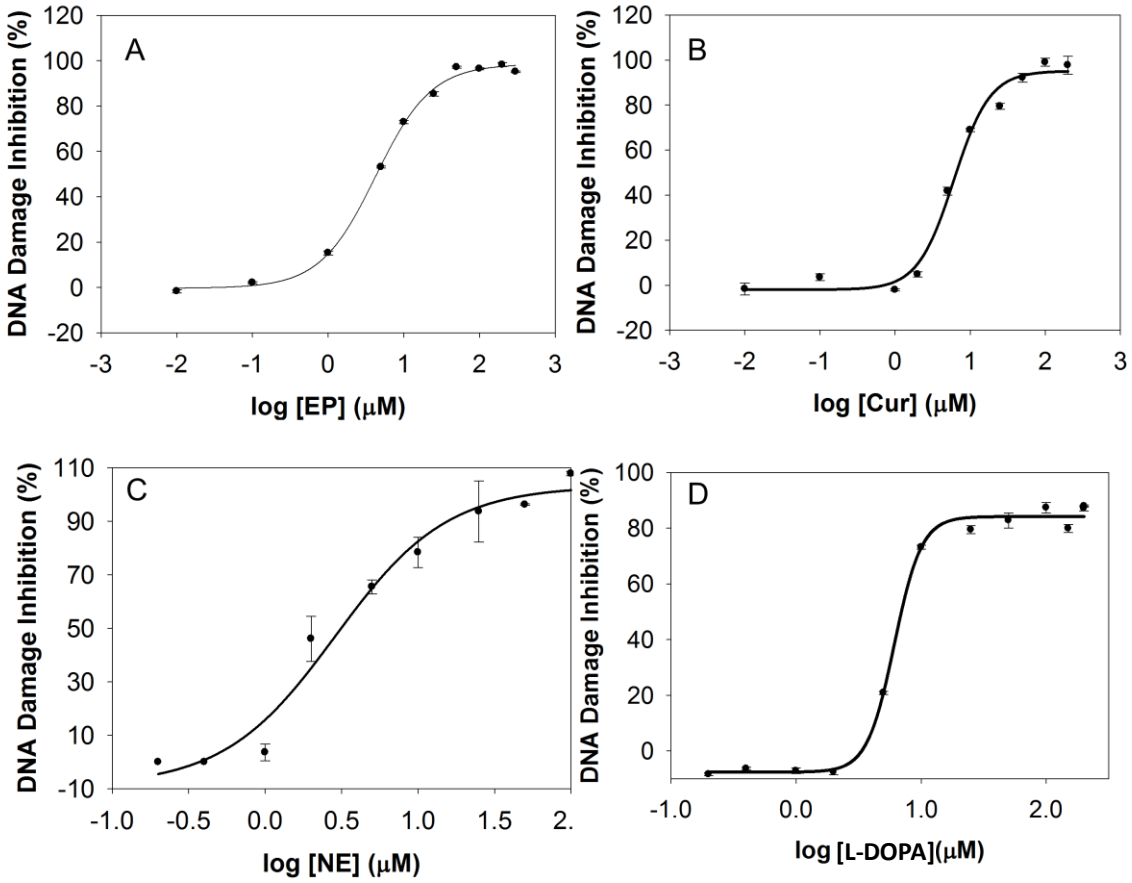

Fig. S8 Dose-response curves showing inhibition of Fe^{2+}/H_2O_2-mediated DNA damage by A) epinephrine (EP), B) curcumin (Cur) , C) norepinephrine (NE), and D) *l*-dihydroxyphenylalanine (L-DOPA) in MES buffer (10 mM, pH 6.0). Error bars represent standard deviations from three trials.

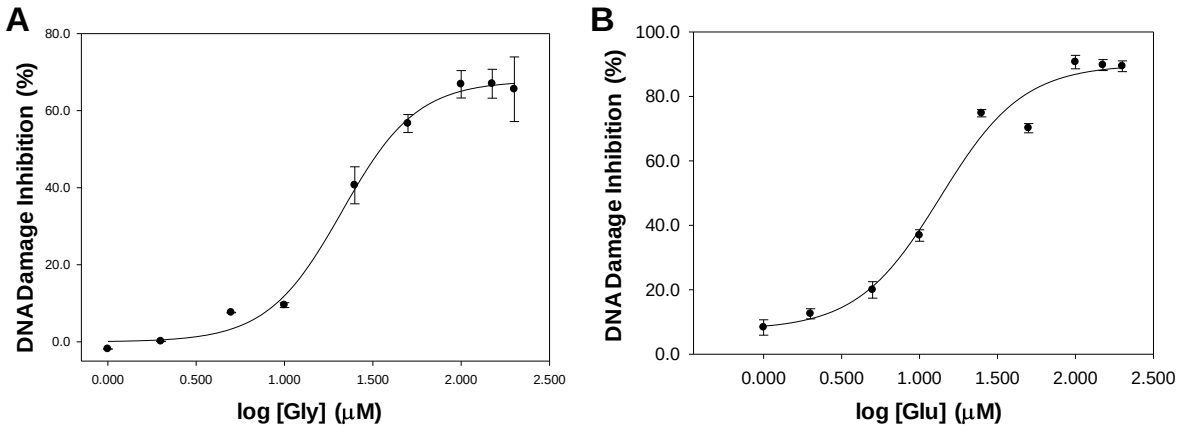

Fig. S9 Dose-response curves showing inhibition of Cu^{+}/H_2O_2-mediated DNA damage by A) glycine (Gly) and B) glutamate (Glu) in MOPS buffer (10 mM, pH 7.0). Error bars represent standard deviations calculated from three trials.

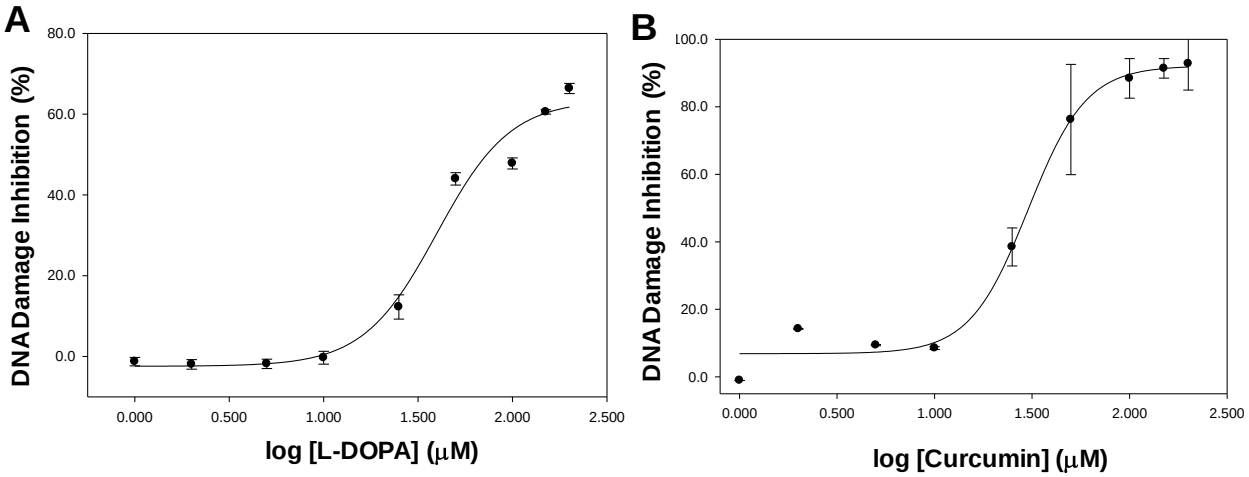

Fig. S10 Dose-response curves showing inhibition of Cu^{+}/H_2O_2-mediated DNA damage by A) *l*-dihydroxyphenylalanine (L-DOPA) and B) curcumin in MOPS buffer (10 mM, pH 7.0). Error bars represent standard deviations of three trials.

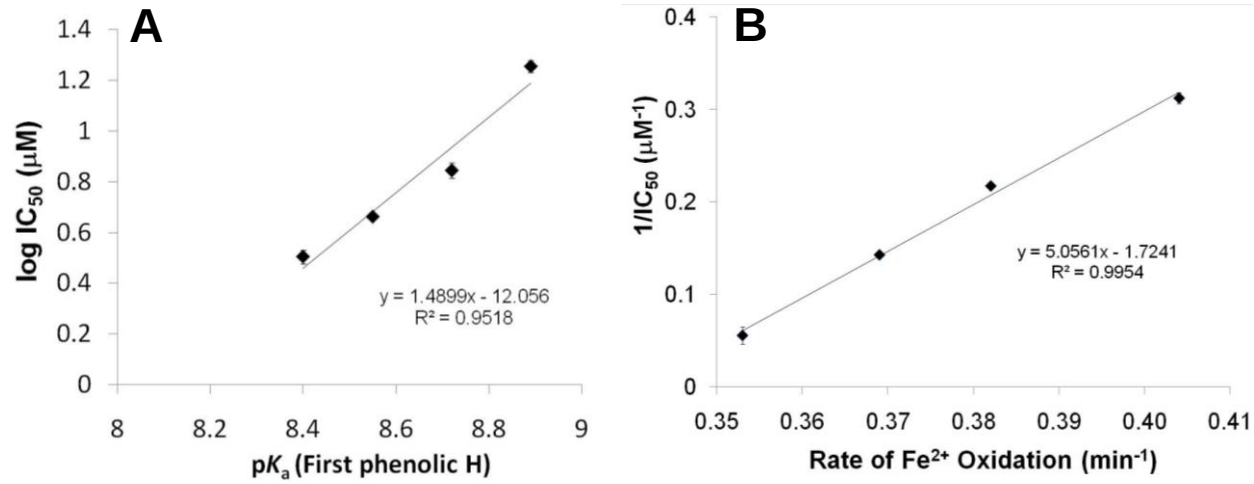

Fig. S11 A) Graph of log IC_{50} for catecholamine (DA, EP, NE, and L-DOPA) prevention of iron-mediated DNA damage vs. pK_a of the first phenolic H atom with the linear fit shown. B) Graph of $1/IC_{50}$ vs. initial rate of Fe^{2+} oxidation in the presence of the four catecholamines with the linear fit shown.

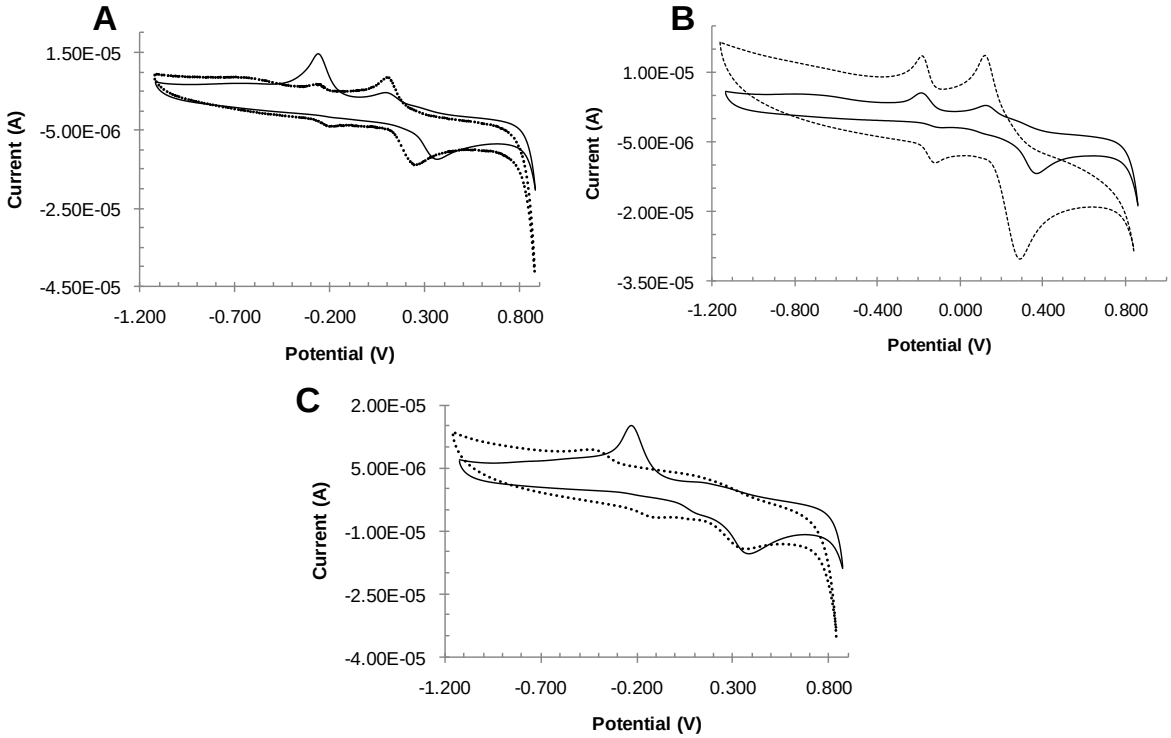

Fig. S12 Cyclic voltammograms vs. NHE for A) dopamine, B) norepinephrine, and C) *l*-dihydroxyphenylalanine (L-DOPA; 380 µM, dotted line) and 10 min after addition of $FeSO_4$ (380 µM; solid line) in MES buffer (64 mM, pH 6.0) with KNO_3 (64 mM) as a supporting electrolyte.

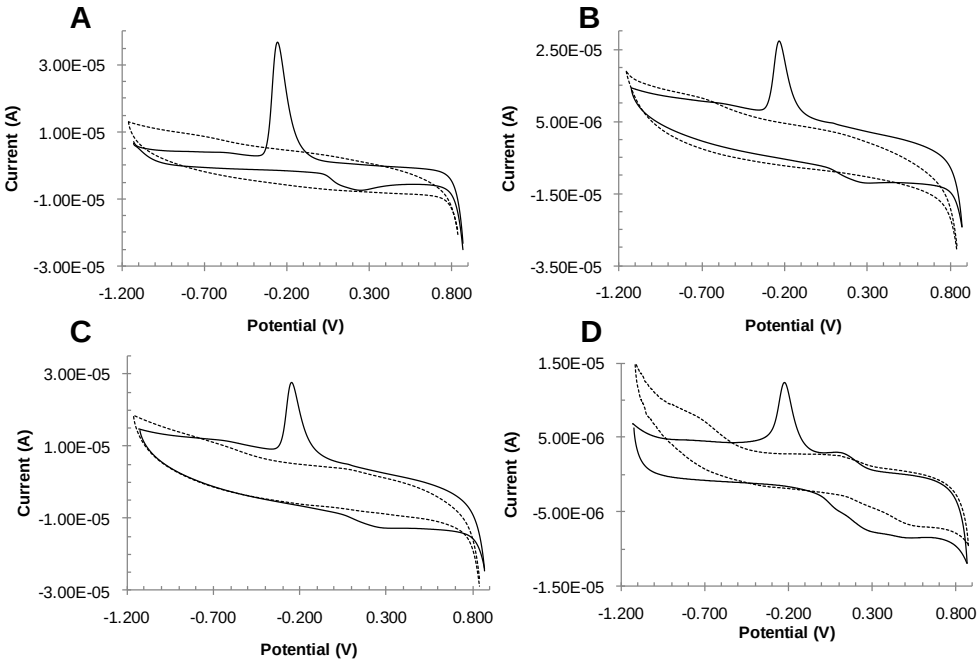

Fig. S13 Cyclic voltammograms vs. NHE for A) glycine, B) glutamate, C) 4-aminobutyrate, and D) curcumin (380 µM, dotted line) and 10 min after addition of $FeSO_4$ (380 µM; solid line) in MES buffer (64 mM, pH 6.0) with KNO_3 (64 mM) as a supporting electrolyte.

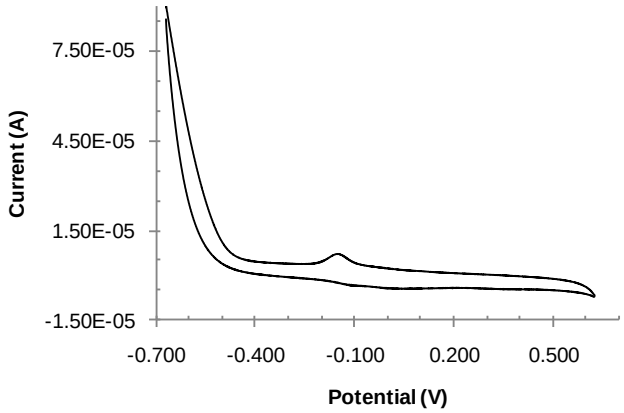

Fig. S14 Cyclic voltammogram vs. NHE of $CuSO_4$ (380 µM) in MOPS buffer (64 mM, pH 7.0) with KNO_3 (64 mM) as a supporting electrolyte.

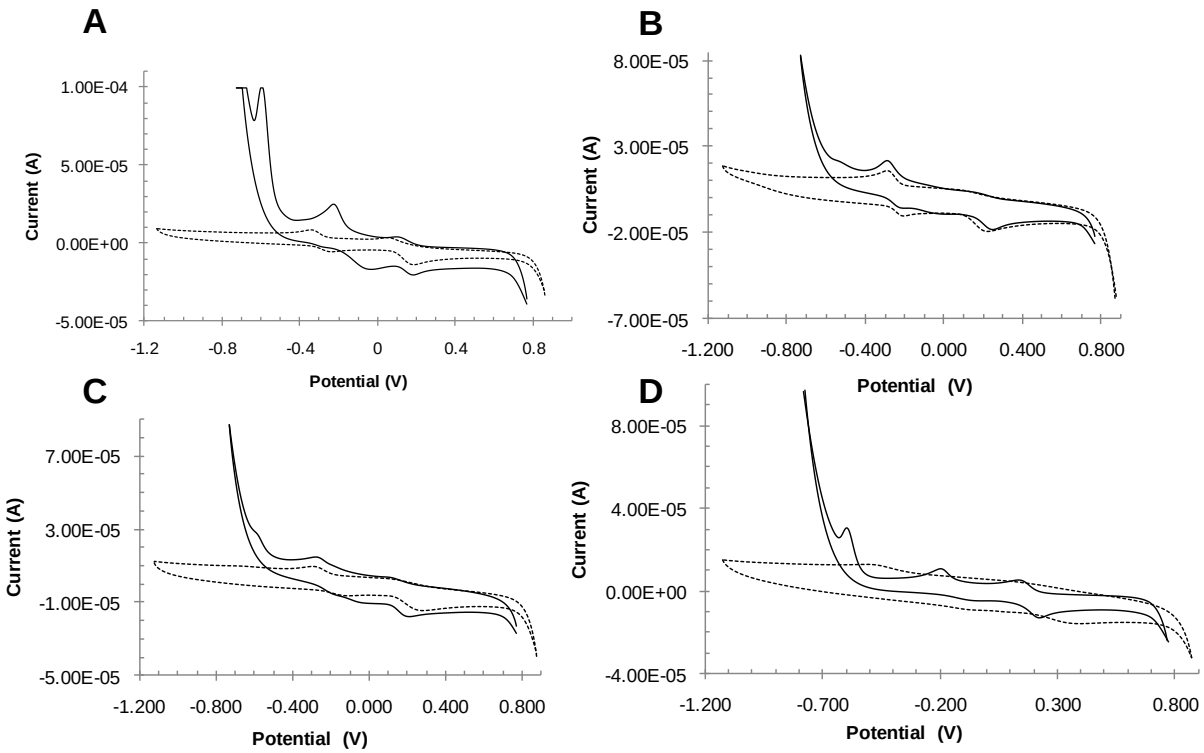

Fig. S15 Cyclic voltammograms vs. NHE for A) dopamine, B) epinephrine, C) norepinephrine, and D) *l*-dihydroxyphenylalanine (L-DOPA; 380 µM, dotted line) and 10 min after addition of $CuSO_4$ (380 µM; solid line) in MOPS buffer (64 mM, pH 7.0) with KNO_3 (64 mM) as a supporting electrolyte.

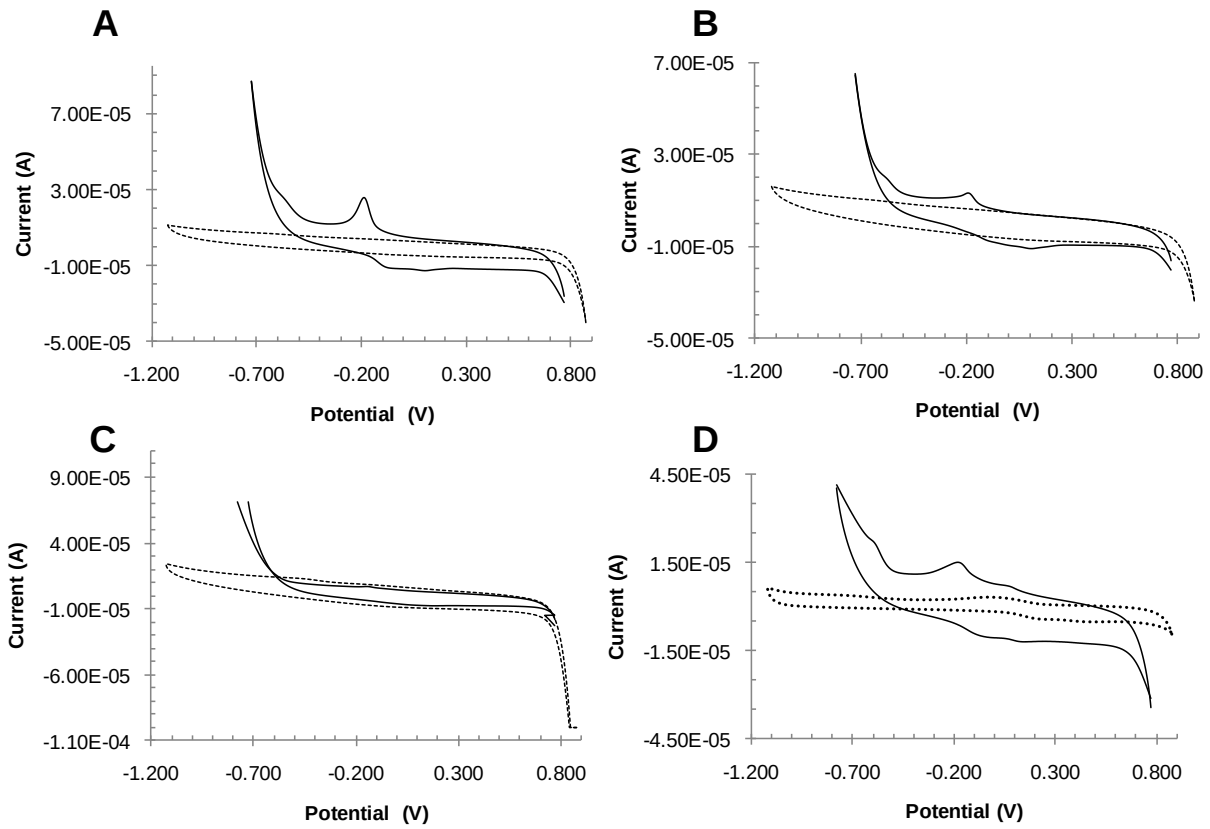

Fig. S16 Cyclic voltammograms vs. NHE for A) glycine, B) glutamate, C) 4-aminobutyrate, and D) curcumin (380 µM, dotted line) and 10 min after addition of $CuSO_4$ (380 µM; solid line) in MOPS buffer (64 mM, pH 7.0) with KNO_3 (64 mM) as a supporting electrolyte.

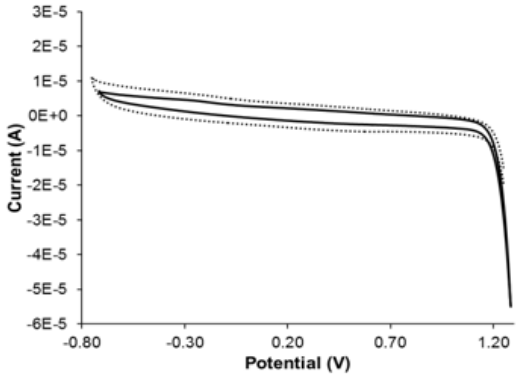

Fig. S17 Cyclic voltammograms vs. NHE for tartrate (145 µM) in MES buffer (64 mM, pH 6.0; dotted line) or MOPS buffer (64 mM, pH 7.2; solid line) with KNO_3 (64 mM) as a supporting electrolyte.

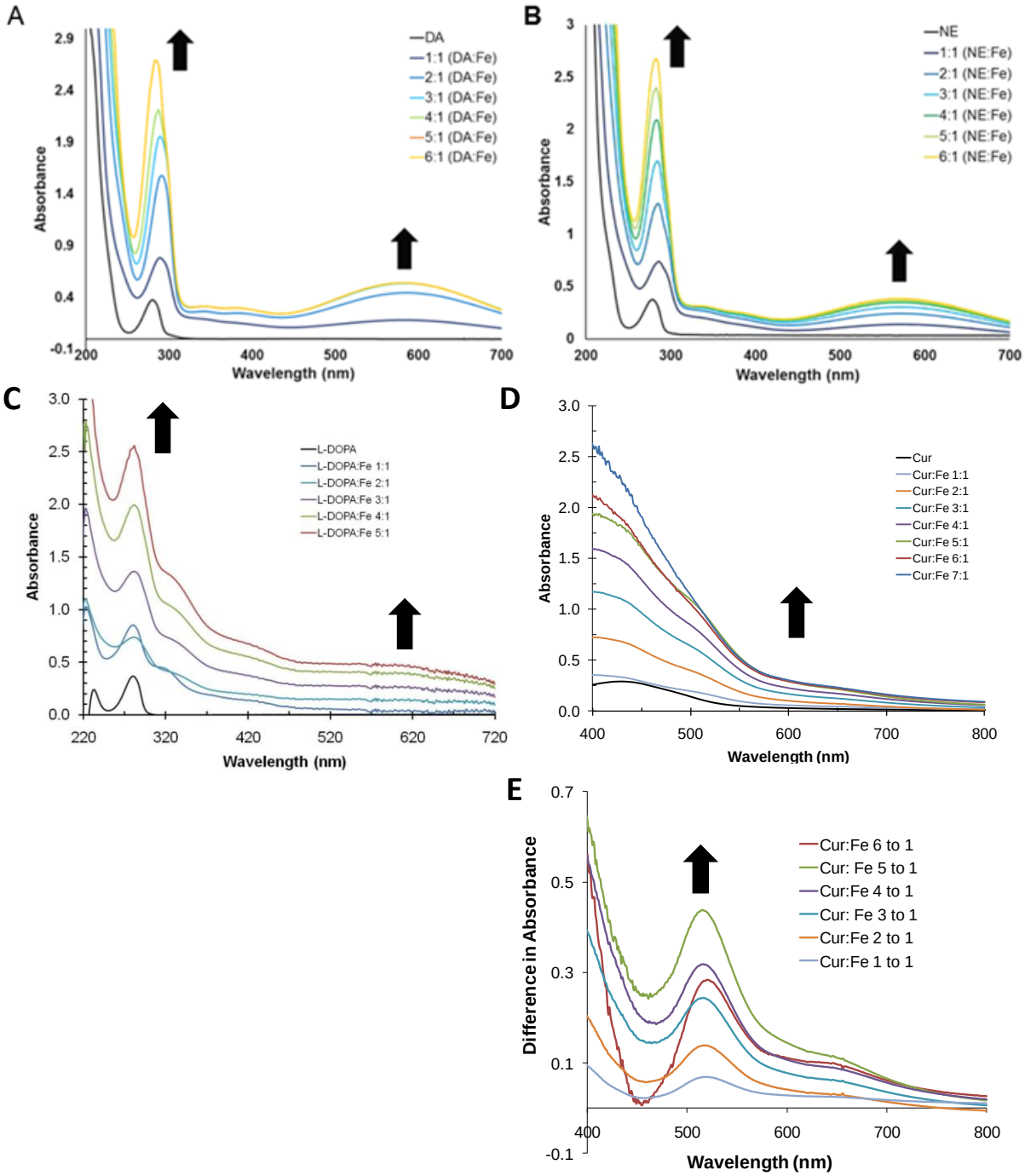

Fig. S18 UV-vis spectra of A) dopamine (DA), B) norepinephrine (NE), C) *l*-dihydroxyphenylalanine (L-DOPA) and D) curcumin (Cur) with Fe^{2+}. A 1:1 ratio in A), B), and C) represents 145 µM Fe^{2+} and compound, and higher ratios are obtained by increasing concentrations of DA, NE and L-DOPA with a fixed Fe^{2+} concentration. A 1:1 ratio in D) represents 29 µM Fe^{2+} and curcumin, and higher ratios are obtained by increasing concentrations of curcumin with a fixed Fe^{2+} concentration (29 µM). B) difference spectra of D, subtracting out contributions from curcumin. Reaction times were 10 min in MES buffer (pH 6.0, 25 mM). Fe^{2+} solutions show no significant absorbance at these wavelengths.

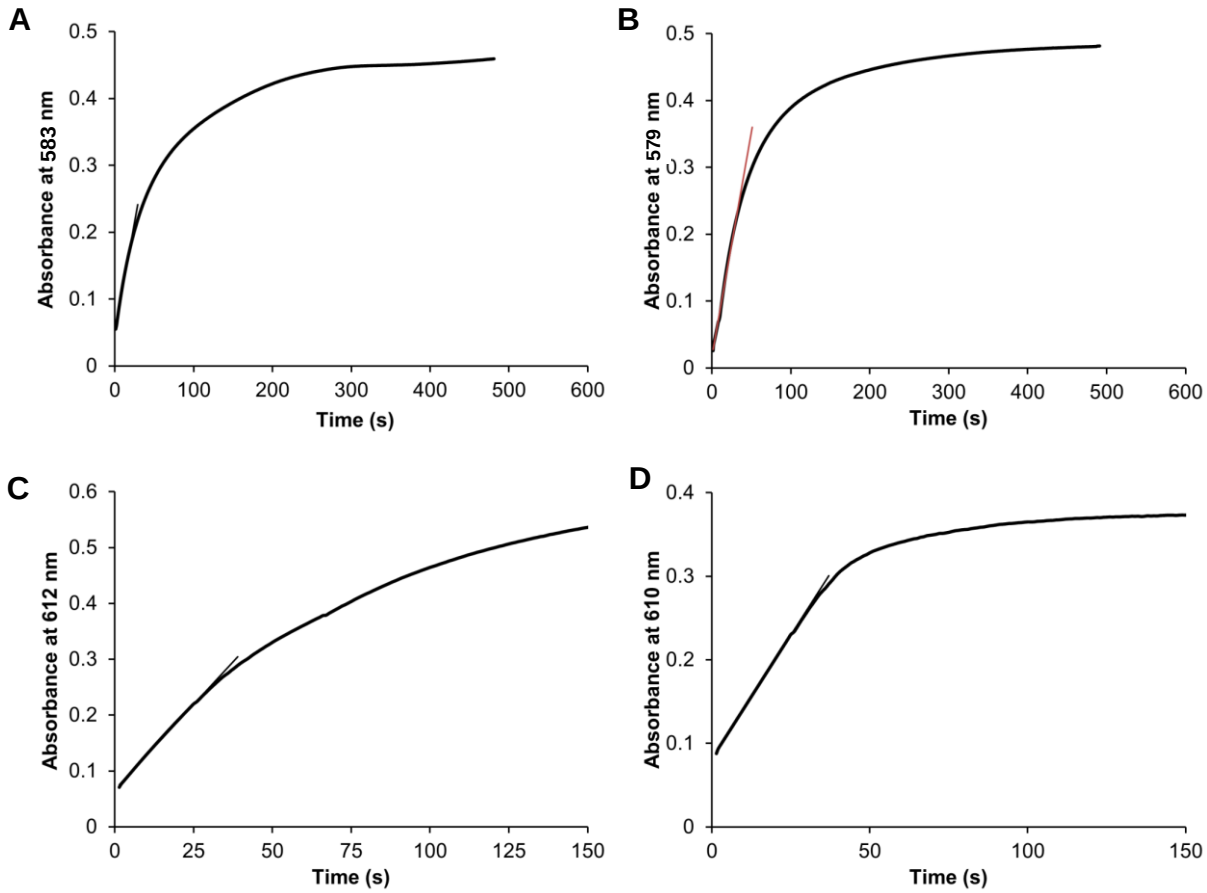

Fig. S19 Absorbance versus time graphs for 3:1 molar ratios of A) dopamine (DA, y = 0.39 x + 0.011, R^2 = 0.995), B) norepinephrine (NE, y = 0.39 x + 0.011, R^2 = 0.995), C) *l*-dihydroxyphenylalanine (L-DOPA, y = 0.39 x + 0.011, R^2 = 0.995), and D) curcumin (y = 0.39 x + 0.011, R^2 = 0.995) with Fe^{2+}. The slope of the best fit line represents the initial rate of Fe^{2+} oxidation.

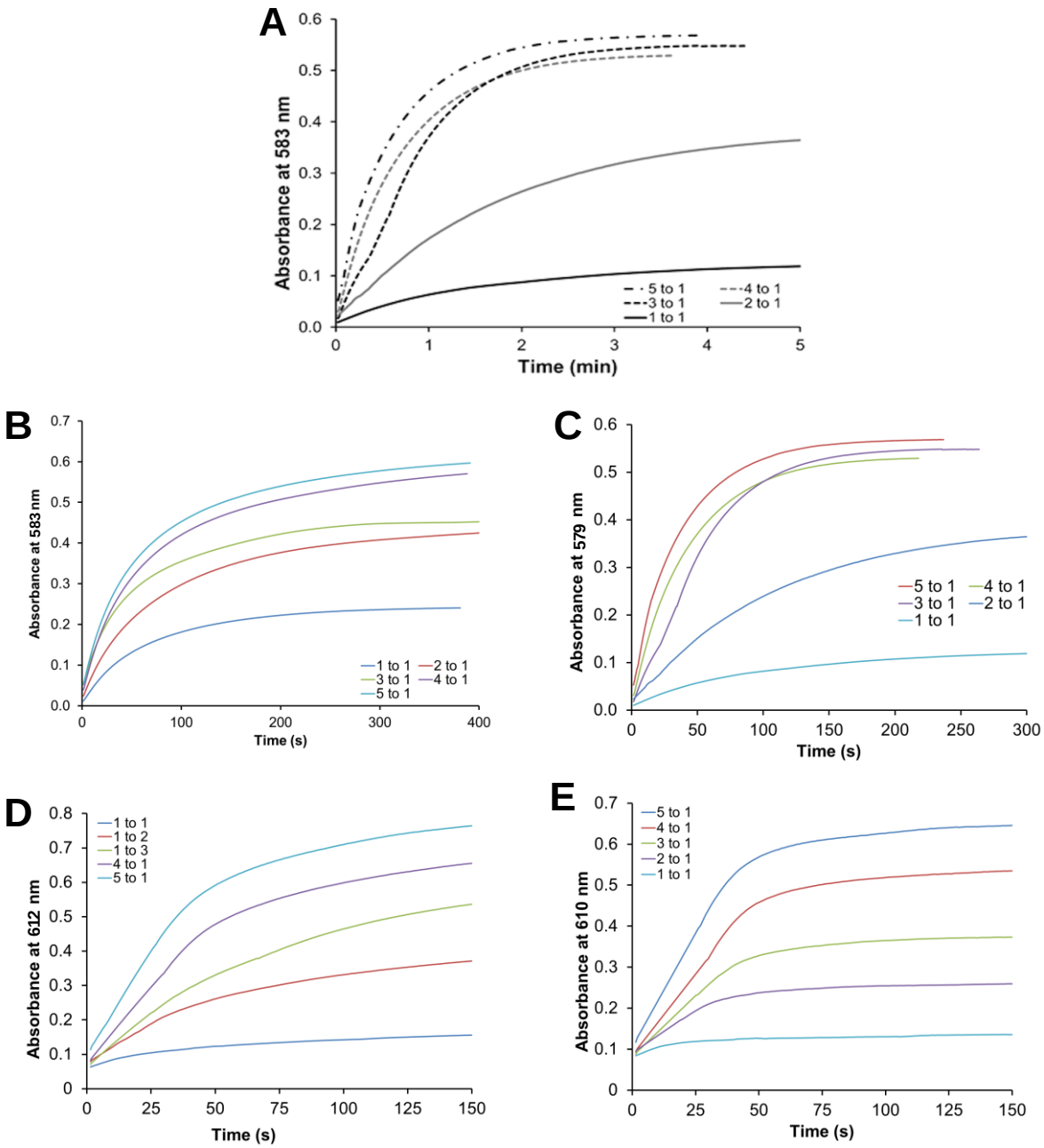

Fig. S20 Absorbance vs. time spectra for A) epinephrine (EP), B) dopamine (DA), C) norepinephrine (NE), D) *l*-dihydroxyphenylalanine (L-DOPA), and E) curcumin with Fe^{2+}. A 1:1 ratio represents 145 µM Fe^{2+} and compound, and higher ratios are obtained by increasing concentrations of EP, DA, NE, and L-DOPA with a fixed Fe^{2+} concentration (145 µM). A 1:1 ratio represents 29 µM Fe^{2+} and curcumin and higher ratios are obtained by increasing concentrations of curcumin with a fixed Fe^{2+} concentration (29 µM). Reaction times were 30 min in MES buffer (pH 6.0; 25 mM).

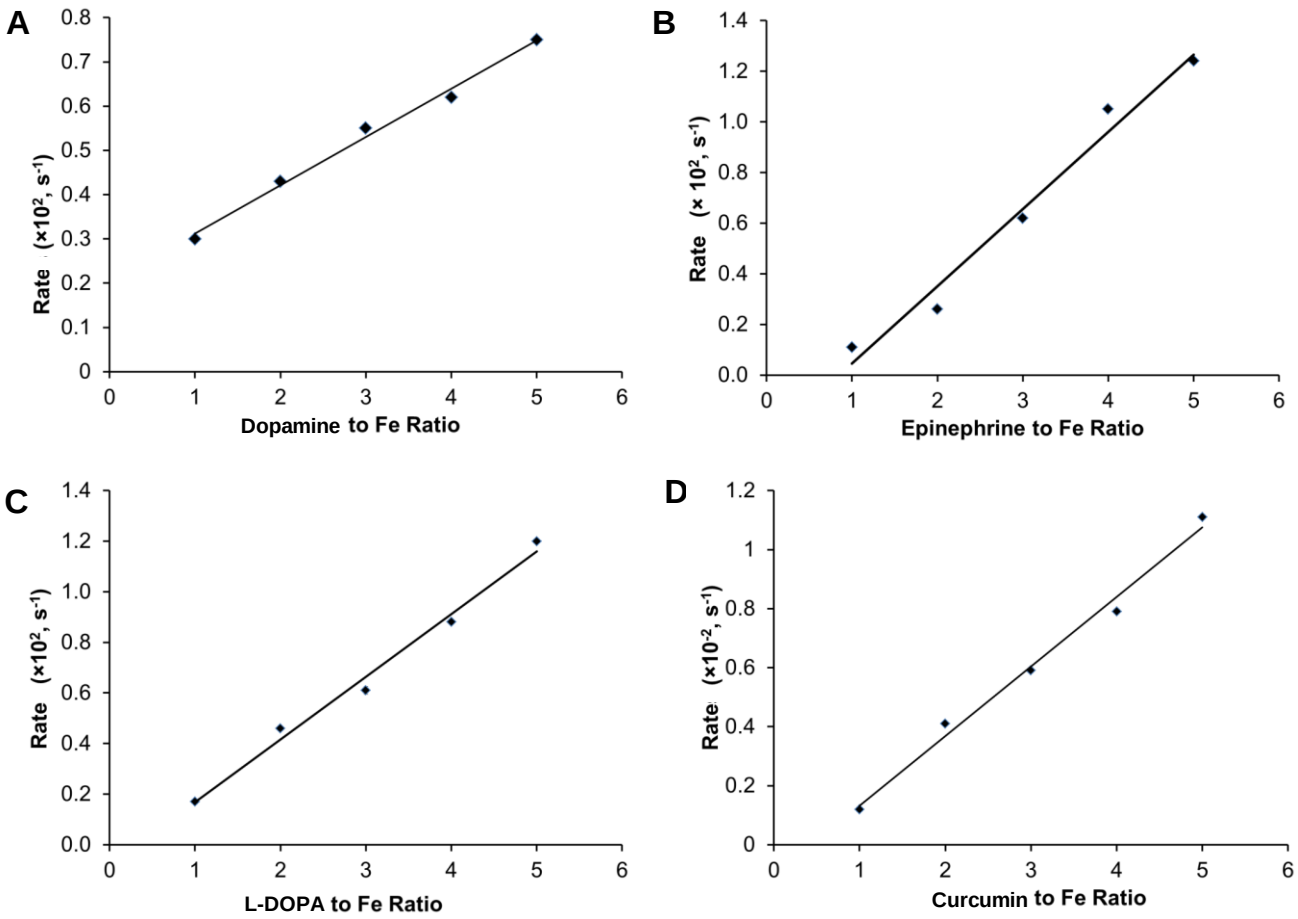

Fig. S21 Graphs of Fe^{2+} oxidation rate vs. molar ratio of A) dopamine (DA), B) norepinephrine (NE), C) *l*-dihydroxyphenylalanine (L-DOPA), and D) curcumin with Fe^{2+}. Error bars are within marker size.

Table S27 Tabulation of initial Fe^{2+} oxidation rates for catecholamines and curcumin.

	Norepinephrine	**Dopamine**	**Epinephrine**	**L-DOPA**	**Curcumin[a]**
Molar ratio of ligand to Fe^{2+}	**Rate ($\times 10^{-2}$ min^{-1})**	**Rate ($\times 10^{-2}$ min^{-1})**	**Rate ($\times 10^{-2}$ min^{-1})**	**Rate ($\times 10^{-2}$ min^{-1})**	**Rate ($\times 10^{-2}$ min^{-1})**
1	21.60 ± 0.001	0.300 ± 0.007	0.110 ± 0.001	0.170 ± 0.004	0.120 ± 0.001
2	32.40 ± 0.006	0.430 ± 0.005	0.260 ± 0.002	0.460 ± 0.009	0.410 ± 0.008
3	40.20 ± 0.003	0.550 ± 0.002	0.620 ± 0.003	0.61 ± 0.02	0.59 ± 0.01
4	45.60 ± 0.007	0.620 ± 0.002	1.050 ± 0.006	0.880 ± 0.008	0.790 ± 0.009
5	51.60 ± 0.008	0.750 ± 0.001	1.240 ± 0.003	1.20 ± 0.01	1.11 ± 0.01

[a]Curcumin data was obtained with 29 μM Fe^{2+} and varying concentrations of curcumin (29-145 μM).

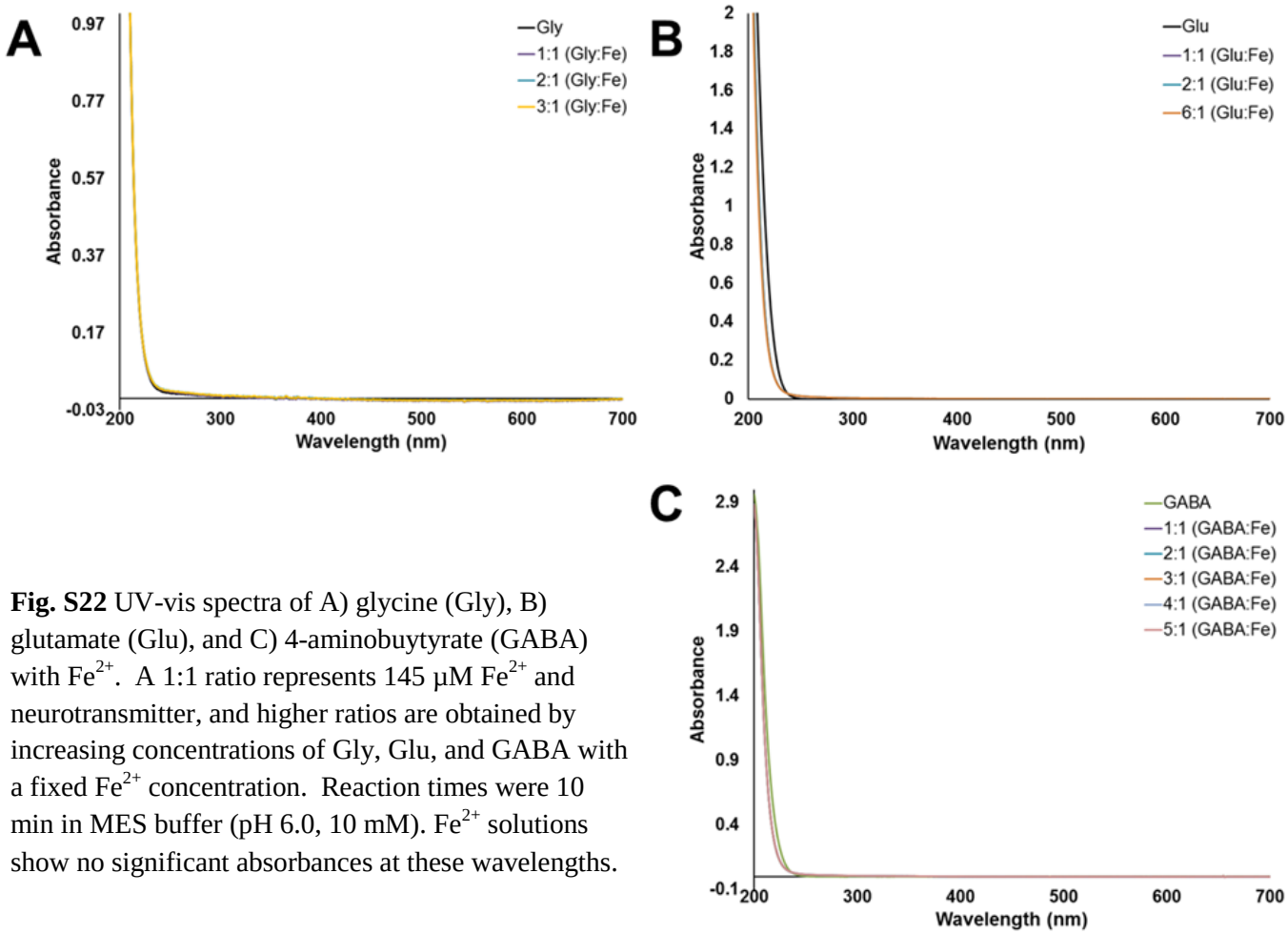

Fig. S22 UV-vis spectra of A) glycine (Gly), B) glutamate (Glu), and C) 4-aminobuytyrate (GABA) with Fe^{2+}. A 1:1 ratio represents 145 µM Fe^{2+} and neurotransmitter, and higher ratios are obtained by increasing concentrations of Gly, Glu, and GABA with a fixed Fe^{2+} concentration. Reaction times were 10 min in MES buffer (pH 6.0, 10 mM). Fe^{2+} solutions show no significant absorbances at these wavelengths.

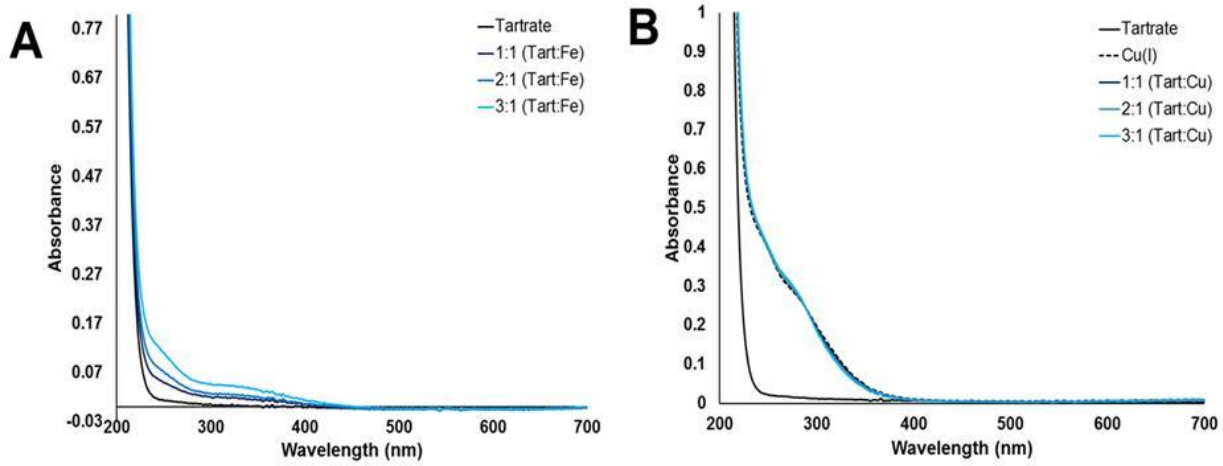

Fig. S23 UV-vis spectra of tartrate (145 µM) with Fe^{2+} and Cu^{+} in A) MES buffer (pH 6.0, 10 mM) with Fe^{2+} and B) MOPS buffer (pH 7.0, 10 mM) with Cu^{+}. A 1:1 ratio represents 145 µM tartrate to 145 µM Fe^{2+} or Cu^{+}, respectively, and higher concentration ratios are obtained by increasing tartrate concentrations with fixed Fe^{2+} and Cu^{+} concentrations (145 µM). Fe^{2+} solutions show no significant absorbances at these wavelengths.

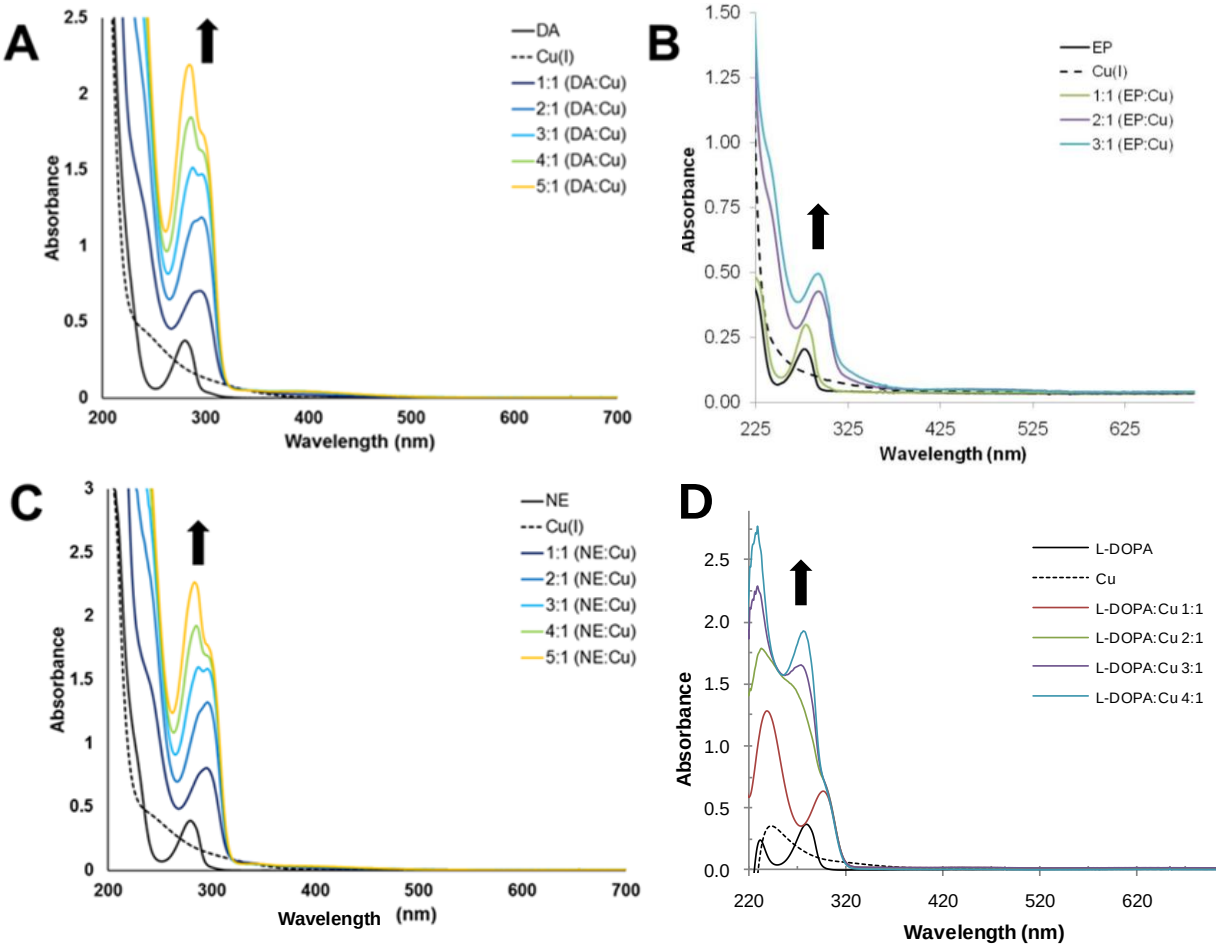

Fig. S24 UV-vis spectra of A) dopamine (DA), B) epinephrine (EP), C) norepinephrine (NE), and L-DOPA with Cu^{+}. A 1:1 ratio represents 145 µM Cu^{+} and neurotransmitter, and higher ratios are obtained by increasing concentrations of DA, EP, NE, and L-DOPA with a fixed Cu^{+} concentration (145 µM). Reaction times were 10 min in MOPS buffer (pH 7.0, 10 mM).

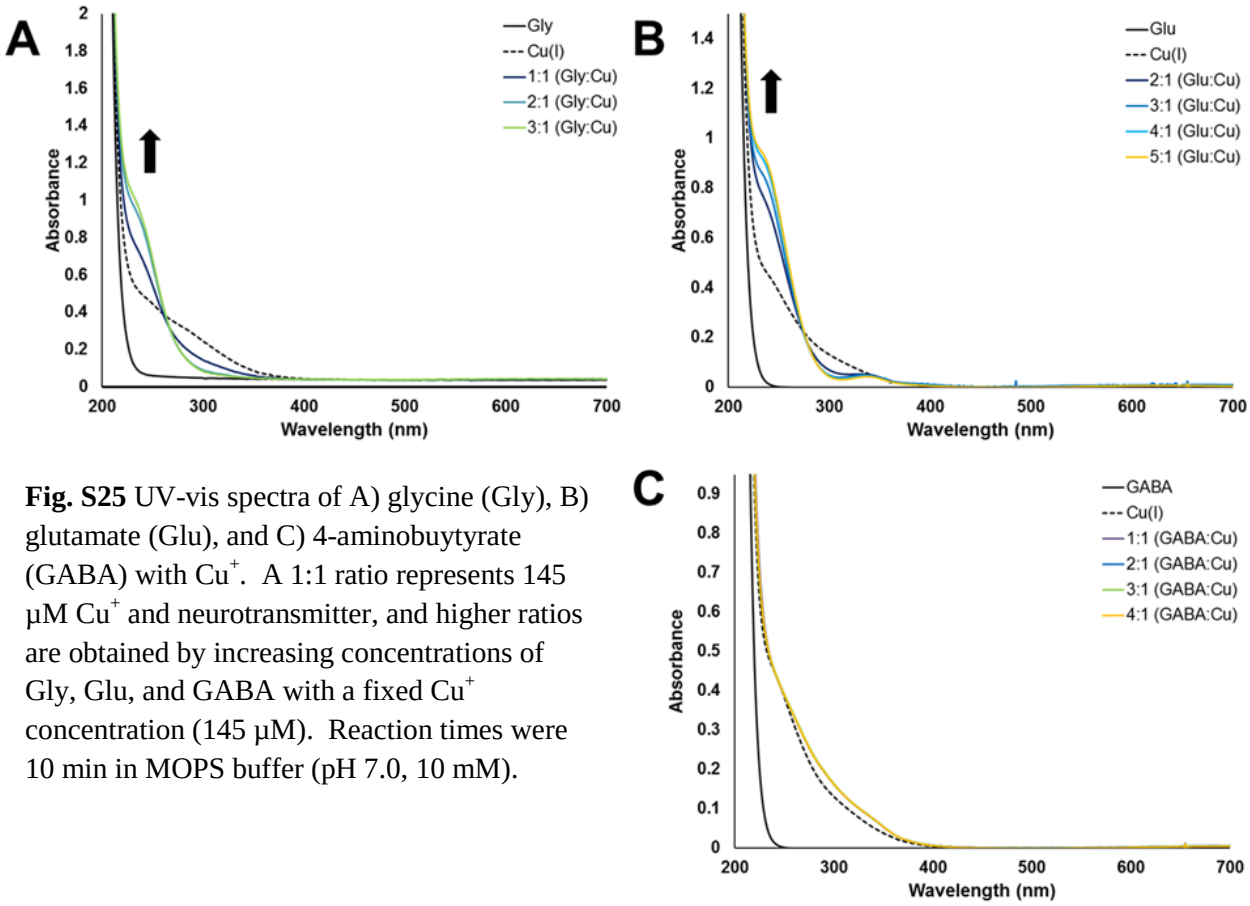

Fig. S25 UV-vis spectra of A) glycine (Gly), B) glutamate (Glu), and C) 4-aminobuytyrate (GABA) with Cu^{+}. A 1:1 ratio represents 145 µM Cu^{+} and neurotransmitter, and higher ratios are obtained by increasing concentrations of Gly, Glu, and GABA with a fixed Cu^{+} concentration (145 µM). Reaction times were 10 min in MOPS buffer (pH 7.0, 10 mM).

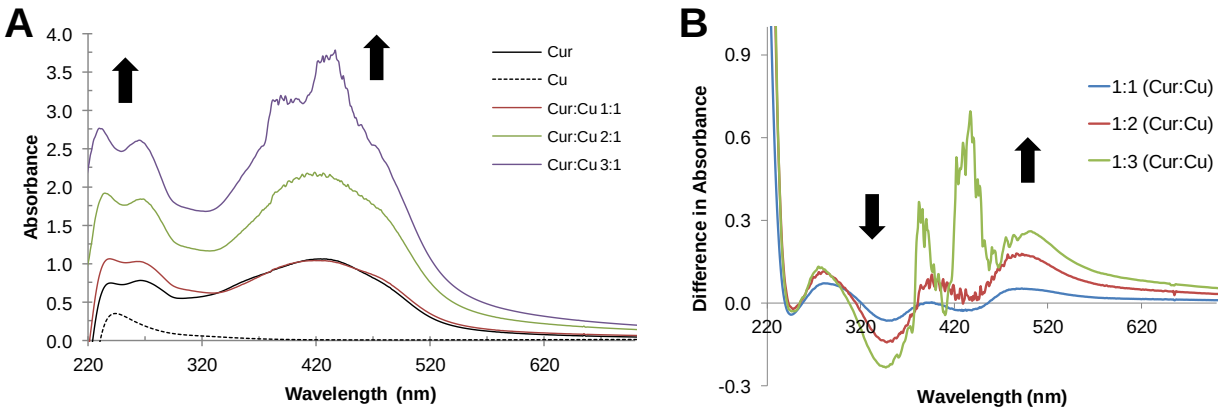

Fig. S26 UV-vis spectra for A) curcumin in the presence of varying Cu^{+} ratios in MOPS buffer (10 mM, pH 7.0) and B) difference spectra of A, subtracting out contributions from curcumin and Cu^{+} only. A 1:1 ratio represents 29 µM Cu^{+} and curcumin, and higher ratios are obtained by increasing concentrations of curcumin with a fixed Cu^{+} concentration (29 µM). Reaction times were 10 min in MOPS buffer (pH 7.0, 10 mM).