Supporting Information

Near-Infrared Responsive Dopamine/Melatonin Derived Nanocomposites Abrogating In-situ Amyloid Beta Nucleation, Propagation and Ameliorate Neuronal Functions

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NMR Peak Assignments:

1H NMR (dopamine (1 mM), 400 MHz, Deuterium Oxide) δ = 6.77 (d, J=8.1, 1H), 6.71 (d, J=2.1, 1H), 6.63 (dd, J=8.1, 2.2, 1H), 3.09 (t, J=7.2, 2H), 2.74 (t, J=7.2, 2H).

	Name	Shift	Range	H's	Integral	Class	J's
1	E (t)	2.74	2.89-2.52	2	2.07	t	7.20, 7.20
2	D (t)	3.09	3.24-2.93	2	2.11	t	7.18, 7.18
3	C (dd)	6.63	6.68-6.57	1	1.09	dd	2.15, 8.12
4	B (d)	6.71	6.74-6.68	1	0.99	d	2.08
5	A (d)	6.77	6.83-6.74	1	1.00	d	8.08

Table S1: The NMR peaks specific to dopamine (1 mM).

1H NMR (Dopamine (1 mM), sodium periodate (1 mM), 0 min, 400 MHz, Deuterium Oxide) δ = 7.01 (dt, J=10.3, 1.7, 1H), 6.36 (d, J=10.2, 1H), 6.25 (s, 1H), 5.96 (s, 0H), 5.68 (s, 0H), 3.82 (t, J=5.2, 0H), 3.18 (q, J=9.2, 8.4, 2H), 2.72 (t, J=7.5, 2H), 2.10 (s, 0H), 1.04 (d, J=6.6, 0H).

	Name	Shift	Range	H's	Integral	Class	J's
1	J (d)	1.04	1.15-0.93	0	0.12	d	6.57
2	I (s)	2.10	2.23 -1.97	0	0.20	s	
3	H (t)	2.72	2.85- 2.44	2	2.13	t	7.50, 7.50
4	G (q)	3.18	3.38-2.87	2	2.47	q	8.37, 8.37, 9.18
5	F (t)	3.82	4.03-3.69	0	0.12	t	5.20, 5.20
6	E (s)	5.68	5.82-5.58	0	0.05	s	
7	D (s)	5.96	6.01-5.92	0	0.10	s	
8	C (s)	6.25	6.29-6.04	1	1.22	s	
9	B (d)	6.36	6.52-6.30	1	1.17	d	10.23
10	A (dt)	7.01	7.14-6.88	1	1.00	dt	1.71, 1.71, 10.27

Table S2: The NMR resonance peak shifts of dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 0 min.

1H NMR (Dopamine (1 mM), sodium periodate (1 mM), 30 min, 400 MHz, Deuterium Oxide) δ = 7.11 – 6.91 (m, 1H), 6.36 (d, J=10.2, 1H), 6.25 (s, 1H), 5.98 (d, J=16.2, 0H), 5.69 (s, 0H), 5.36 (s, 0H), 3.82 (t, J=5.2, 0H), 3.52 (d, J=6.9, 0H), 3.38 – 2.82 (m, 3H), 2.80 – 2.42 (m, 2H), 2.10 (s, 0H), 1.04 (d, J=6.6, 0H).

	Name	Shift	Range	H's	Integral	Class	J's
1	L (d)	1.04	1.29-0.91	0	0.12	d	6.56
2	K (s)	2.10	2.25-1.94	0	0.25	s	
3	J (m)	2.72	2.80 -2.42	2	2.24	m	
4	I (m)	3.19	3.38-2.82	3	2.83	m	
5	H (d)	3.52	3.60-3.46	0	0.02	d	6.90
6	G (t)	3.82	3.93 - 3.72	0	0.14	t	5.18, 5.18
7	F (s)	5.36	5.51- 5.29	0	0.02	s	
8	E (s)	5.69	5.75 -5.60	0	0.06	s	
9	D (d)	5.98	6.04- 5.89	0	0.14	d	16.19
10	C (s)	6.25	6.29 - 6.05	1	1.22	s	
11	B (d)	6.36	6.51- 6.30	1	1.21	d	10.25
12	A (m)	7.01	7.11- 6.91	1	1.00	m	

Table S3: The NMR resonance peak shifts of dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 30 min.

1H NMR (Dopamine (1 mM), sodium periodate (1 mM), 60 min, 400 MHz, Deuterium Oxide) δ = 7.19 – 6.83 (m, 1H), 6.36 (d, J=10.2, 1H), 6.30 – 5.89 (m, 1H), 5.69 (s, 0H), 5.37 (s, 0H), 3.82 (t, J=5.2, 0H), 3.46 – 2.83 (m, 3H), 2.72 (t, J=7.5, 2H), 2.10 (d, J=1.4, 0H), 1.04 (d, J=6.5, 0H).

	Name	Shift	Range	H's	Integral	Class	J's
1	J (d)	1.04	1.16 -0.83	0	0.13	d	6.52
2	I (d)	2.10	2.30 - 1.94	0	0.26	d	1.36
3	H (t)	2.72	2.80 - 2.47	2	2.42	t	7.48, 7.48
4	G (m)	3.14	3.46 - 2.83	3	3.04	m	
5	F (t)	3.82	3.92 - 3.66	0	0.15	t	5.23, 5.23
6	E (s)	5.37	5.47 - 5.29	0	0.03	s	
7	D (s)	5.69	5.80 - 5.62	0	0.05	s	
8	C (m)	6.10	6.30 - 5.89	1	1.45	m	
9	B (d)	6.36	6.57 - 6.30	1	1.35	d	10.23
10	A (m)	7.01	7.19 - 6.83	1	1.00	m	

Table S4: The NMR resonance peak shifts of dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 60 min.

1H NMR (dopamine (1 mM), sodium periodate (1 mM), 120 min, 400 MHz, Deuterium Oxide) δ = 7.01 (dd, J=10.2, 2.0, 1H), 6.36 (d, J=10.3, 1H), 6.25 (s, 1H), 5.95 (s, 0H), 5.69 (s, 0H), 3.82 (t, J=5.3, 0H), 3.33 – 2.89 (m, 3H), 2.83 – 2.46 (m, 2H), 2.10 (d, J=1.3, 0H), 1.04 (d, J=6.5, 0H).

	Name	Shift	Range	H's	Integral	Class	J's
1	J (d)	1.04	1.21-0.86	0	0.14	d	6.53
2	I (d)	2.10	2.19-1.92	0	0.27	d	1.26
3	H (m)	2.72	2.83-2.46	2	2.34	m	
4	G (m)	3.19	3.33-2.89	3	2.74	m	
5	F (t)	3.82	4.02-3.62	0	0.15	t	5.30, 5.30
6	E (s)	5.69	5.73-5.60	0	0.03	s	
7	D (s)	5.95	6.05-5.91	0	0.11	s	
8	C (s)	6.25	6.27-6.12	1	1.06	s	
9	B (d)	6.36	6.49-6.29	1	1.32	d	10.25
10	A (dd)	7.01	7.08-6.91	1	1.00	dd	2.01, 10.23

Table S5: The NMR resonance peak shifts of dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 120 min.

1H NMR (Melatonin (1 mM), 400 MHz, Deuterium Oxide) δ = 7.32 (d, J=8.8, 1H), 7.21 – 7.05 (m, 2H), 6.81 (dd, J=8.8, 2.5, 1H), 3.79 (s, 3H), 3.37 (t, J=6.8, 2H), 2.95 – 2.63 (m, 2H), 1.80 (s, 3H).

	Name	Shift	Range	H's	Integral	Class	J's
1	G (s)	1.80	1.97-1.48	3	2.99	s	
2	F (m)	2.83	2.95-2.63	2	2.13	m	
3	E (t)	3.37	3.50-3.22	2	2.03	t	6.81, 6.81
4	D (s)	3.79	3.88-3.60	3	2.96	s	
5	C (dd)	6.81	6.95-6.69	1	1.07	dd	2.47, 8.80
6	B (m)	7.11	7.21-7.05	2	2.11	m	
7	A (d)	7.32	7.42-7.24	1	1.00	d	8.80

Table S6: The NMR resonance peak shifts of melatonin (Mel, 1 mM).

1H NMR (Melatonin (1 mM), Dopamine (1 mM), 400 MHz, Deuterium Oxide) δ = 7.32 (d, J=8.8, 1H), 7.16 – 7.07 (m, 2H), 6.86 – 6.71 (m, 2H), 6.64 (dd, J=8.1, 2.1, 1H), 3.79 (s, 3H), 3.37 (t, J=6.8, 2H), 3.12 (t, J=7.2, 1H), 2.96 – 2.65 (m, 3H), 1.80 (s, 3H).

	Name	Shift	Range	H's	Integral	Class	J's
1	I (s)	1.80	1.89 -1.67	3	3.01	s	
2	H (m)	2.81	2.96 -2.65	3	2.86	m	
3	G (t)	3.12	3.23-3.00	1	1.05	t	7.22, 7.22
4	F (t)	3.37	3.58-3.27	2	2.02	t	6.78, 6.78
5	E (s)	3.79	3.86-3.70	3	2.96	s	
6	D (dd)	6.64	6.70-6.60	1	0.52	dd	2.11, 8.09
7	C (m)	6.79	6.86-6.71	2	2.04	m	
8	B (m)	7.11	7.16-7.07	2	2.00	m	
9	A (d)	7.32	7.36-7.28	1	1.00	d	8.85

Table S7: The NMR resonance peak shifts of melatonin (Mel, 1 mM) with dopamine (DA, 1 mM) mixture

1H NMR (Melatonin (1 mM), Dopamine (1 mM), sodium periodate (1 mM), 0 min, 400 MHz, Deuterium Oxide) δ = 7.31 (d, J=9.5, 1H), 7.20 – 6.95 (m, 3H), 6.92 – 6.69 (m, 2H), 6.43 – 6.11 (m, 1H), 3.79 (d, J=2.2, 4H), 3.37 (t, J=6.9, 2H), 3.28 – 3.13 (m, 1H), 3.08 – 2.67 (m, 4H), 1.80 (d, J=2.3, 3H).

	Name	Shift	Range	H's	Integral	Class	J's
1	I (d)	1.80	2.04-1.59	3	3.32	d	2.25
2	H (m)	2.80	3.08-2.67	4	3.56	m	
3	G (m)	3.18	3.28-3.13	1	0.55	m	
4	F (t)	3.37	3.50-3.31	2	2.37	t	6.89, 6.89
5	E (d)	3.79	3.98-3.64	4	3.76	d	2.18
6	D (m)	6.31	6.43-6.11	1	0.55	m	
7	C (m)	6.78	6.92-6.69	2	1.51	m	
8	B (m)	7.10	7.20-6.95	3	2.64	m	
9	A (d)	7.31	7.40-7.23	1	1.00	d	9.46

Table S8: The NMR resonance peak shifts of melatonin (Mel, 1 mM) with dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 0 min.

1H NMR (Melatonin (1 mM), Dopamine (1 mM), sodium periodate (1 mM), 30 min, 400 MHz, Deuterium Oxide) δ = 7.29 (d, J=8.5, 1H), 7.09 (d, J=5.3, 2H), 6.88 – 6.52 (m, 1H), 6.33 (s, 0H), 5.62 (s, 0H), 3.78 (d, J=4.6, 3H), 3.35 (t, J=6.7, 2H), 3.18 – 2.58 (m, 3H), 1.79 (d, J=4.5, 3H).

	Name	Shift	Range	H's	Integral	Class	J's
1	I (d)	1.79	1.96-1.32	3	2.56	d	4.51
2	H (m)	2.81	3.18-2.58	3	2.87	m	
3	G (t)	3.35	3.48-3.21	2	1.84	t	6.66, 6.66
4	F (d)	3.78	4.00-3.50	3	2.93	d	4.55
5	E (s)	5.62	5.69-5.55	0	0.08	s	
6	D (s)	6.33	6.42-6.08	0	0.22	s	
7	C (m)	6.78	6.88-6.52	1	1.43	m	
8	B (d)	7.09	7.22-6.90	2	1.96	d	5.25
9	A (d)	7.29	7.45-7.24	1	1.00	d	8.51

Table S9: The NMR resonance peak shifts of melatonin (Mel, 1 mM) with dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 30 min.

1H NMR (Melatonin (1 mM), Dopamine (1 mM), sodium periodate (1 mM), 60 min, 400 MHz, Deuterium Oxide) δ = 7.28 (d, J=8.9, 1H), 7.08 (d, J=4.8, 2H), 6.88 – 6.55 (m, 1H), 6.31 (s, 0H), 6.08 (s, 0H), 3.76 (s, 4H), 3.34 (t, J=6.9, 2H), 2.79 (dd, J=13.0, 6.0, 3H), 1.77 (s, 3H).

	Name	Shift	Range	H's	Integral	Class	J's
1	I (s)	1.77	1.94-1.29	3	3.08	s	
2	H (dd)	2.79	3.00-2.62	3	2.57	dd	5.98, 12.96
3	G (t)	3.34	3.47-3.20	2	2.02	t	6.91, 6.91
4	F (s)	3.76	4.00-3.50	4	3.51	s	
5	E (s)	6.08	6.20-5.95	0	0.08	s	
6	D (s)	6.31	6.42-6.23	0	0.10	s	
7	C (m)	6.75	6.88-6.55	1	1.49	m	
8	B (d)	7.08	7.22-6.92	2	2.17	d	4.78
9	A (d)	7.28	7.40-7.23	1	1.00	d	8.86

Table S10: The NMR resonance peak shifts of melatonin (Mel, 1 mM) with dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 60 min.

1H NMR (Melatonin (1 mM), Dopamine (1 mM), sodium periodate (1 mM), 120 min, 400 MHz, Deuterium Oxide) δ = 7.28 (dd, J=9.0, 1.9, 1H), 7.17 (d, J=10.5, 0H), 7.07 (q, J=2.1, 2H), 6.93 – 6.47 (m, 1H), 6.08 (d, J=2.6, 0H), 3.76 (d, J=2.3, 3H), 3.34 (t, J=6.8, 2H), 3.19 – 2.65 (m, 3H), 2.42 (d, J=1.9, 0H), 1.77 (d, J=2.0, 3H).

	Name	Shift	Range	H's	Integral	Class	J's
1	J (d)	1.77	2.02-1.25	3	2.83	d	2.03
2	I (d)	2.42	2.51-2.29	0	0.17	d	1.89
3	H (m)	2.79	3.19-2.65	3	2.71	m	
4	G (t)	3.34	3.46-3.23	2	1.88	t	6.81, 6.81
5	F (d)	3.76	3.92-3.52	3	3.07	d	2.28
6	E (d)	6.08	6.16-5.94	0	0.10	d	2.64
7	D (m)	6.77	6.93-6.47	1	1.48	m	
8	C (q)	7.07	7.12-7.01	2	1.94	q	2.13, 2.13, 2.34
9	B (d)	7.17	7.22-7.14	0	0.19	d	10.53
10	A (dd)	7.28	7.36-7.23	1	1.00	dd	1.87, 8.97

Table S11: The NMR resonance peak shifts of melatonin (Mel, 1 mM) with dopamine (DA, 1 mM) in the presence of sodium periodate ($NaIO_4$, 1 mM) at 120 min.

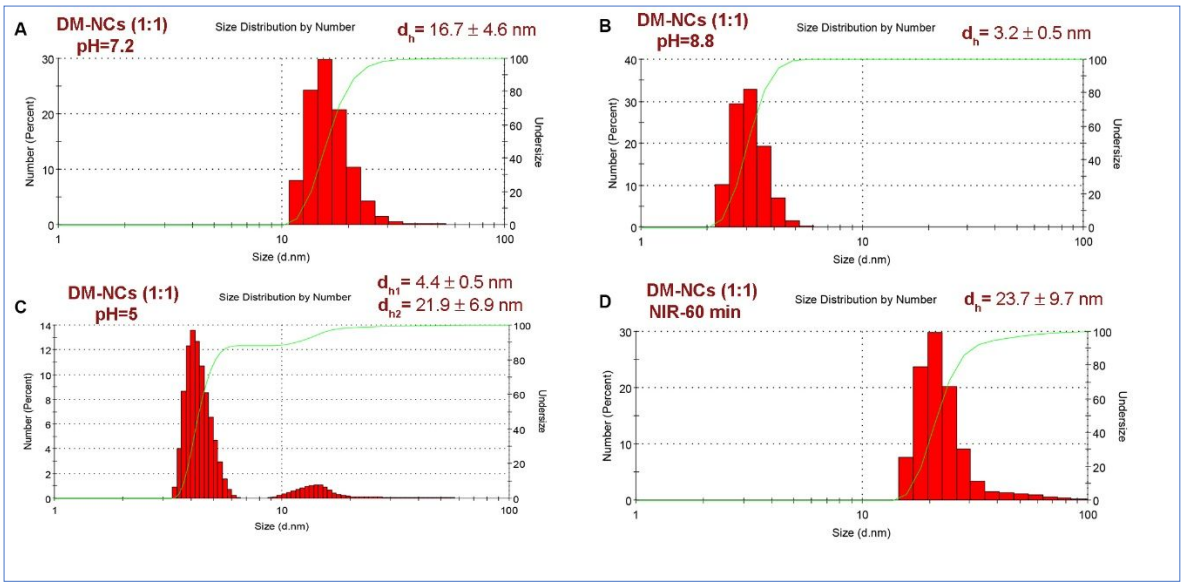

Figure S1. The hydrodynamic particle size distribution of DM-NCs (1:1) at (A) pH=7.2, (B) pH=8.8, (C) pH=5 and (D) upon prolong NIR exposure of 60 min.

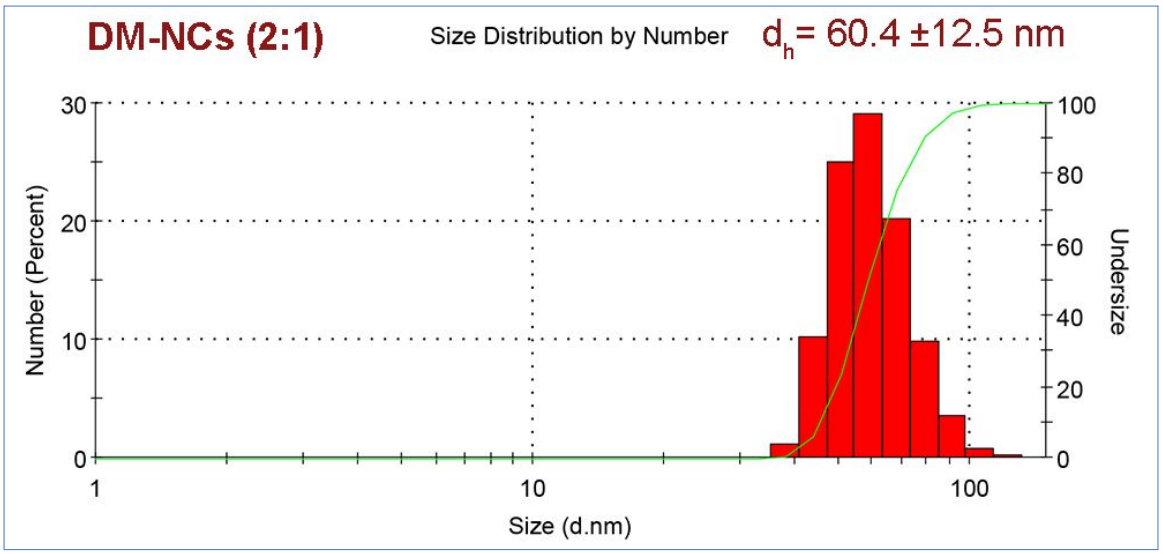

Figure S2. The hydrodynamic particle size distribution of DM-NCs (2:1, DA/Mel) dispersed in the buffer of pH=7.2

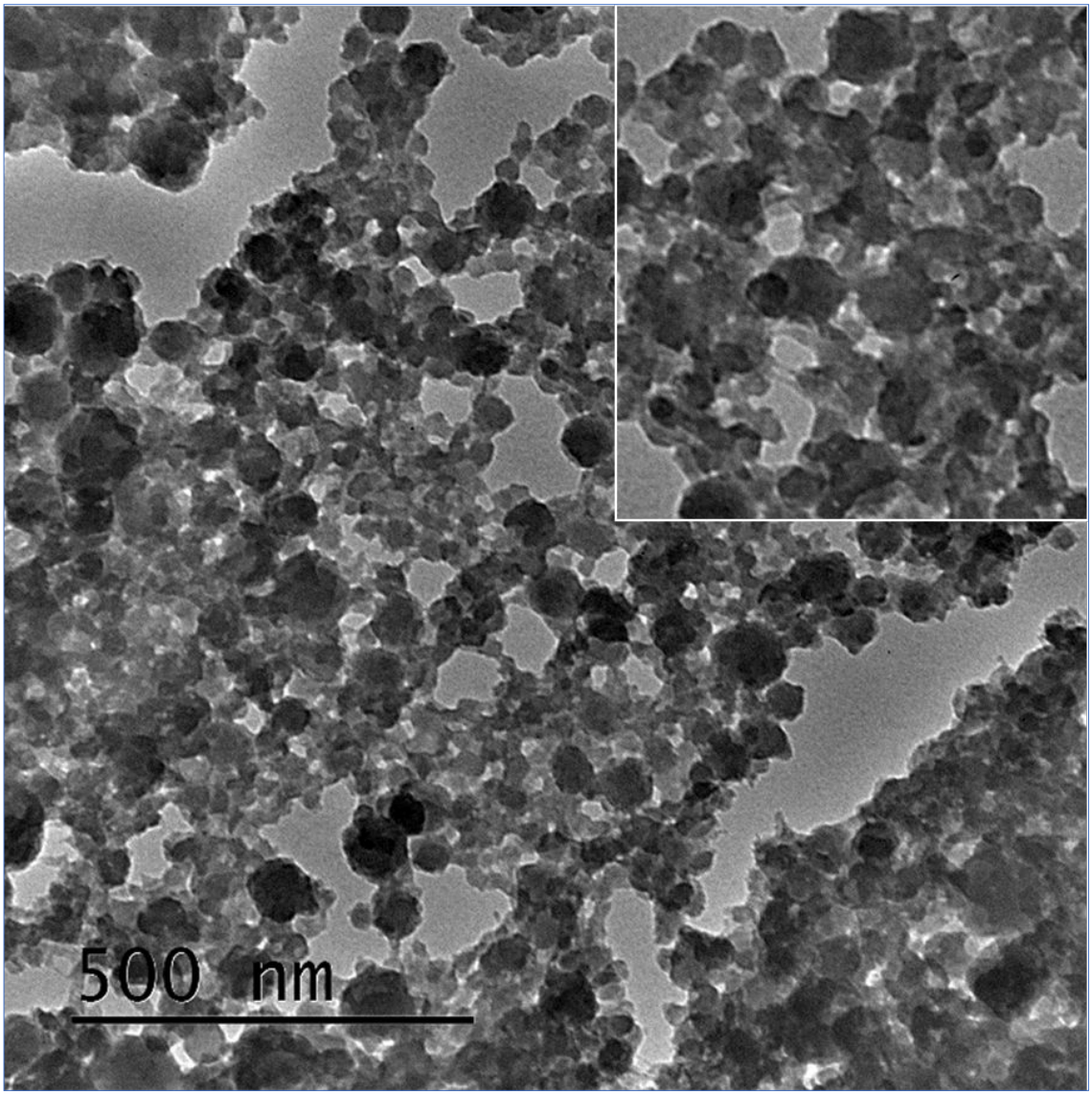

Figure S3. The transmission electron microscopic (TEM) image of the DM-NCs prepared at DA/Mel ratio of 2:1.

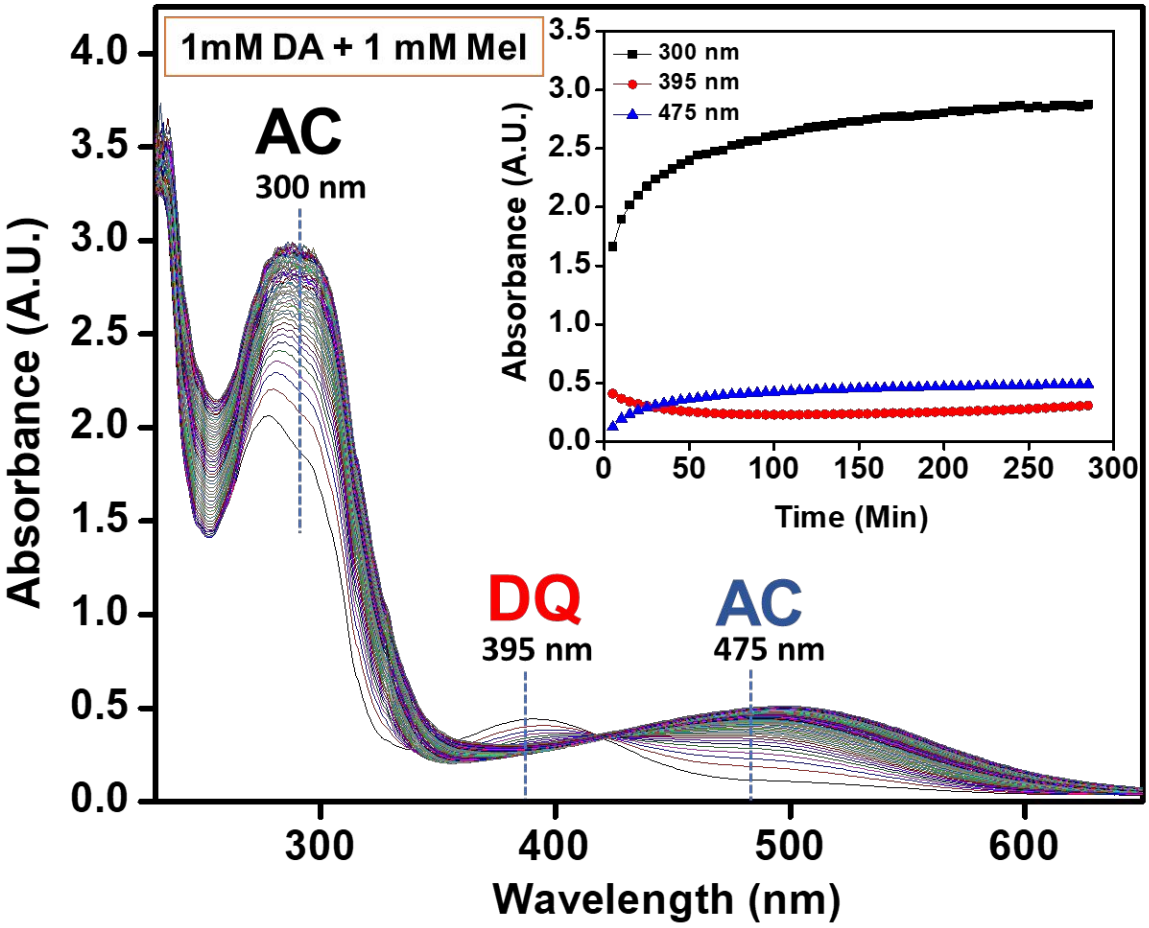

Figure S4. Time-dependent UV-Vis absorbance spectrum of dopamine (DA, 1 mM) and (Mel, 1 mM) added with 1 mM $NaIO_4$ in Milli-Q water.

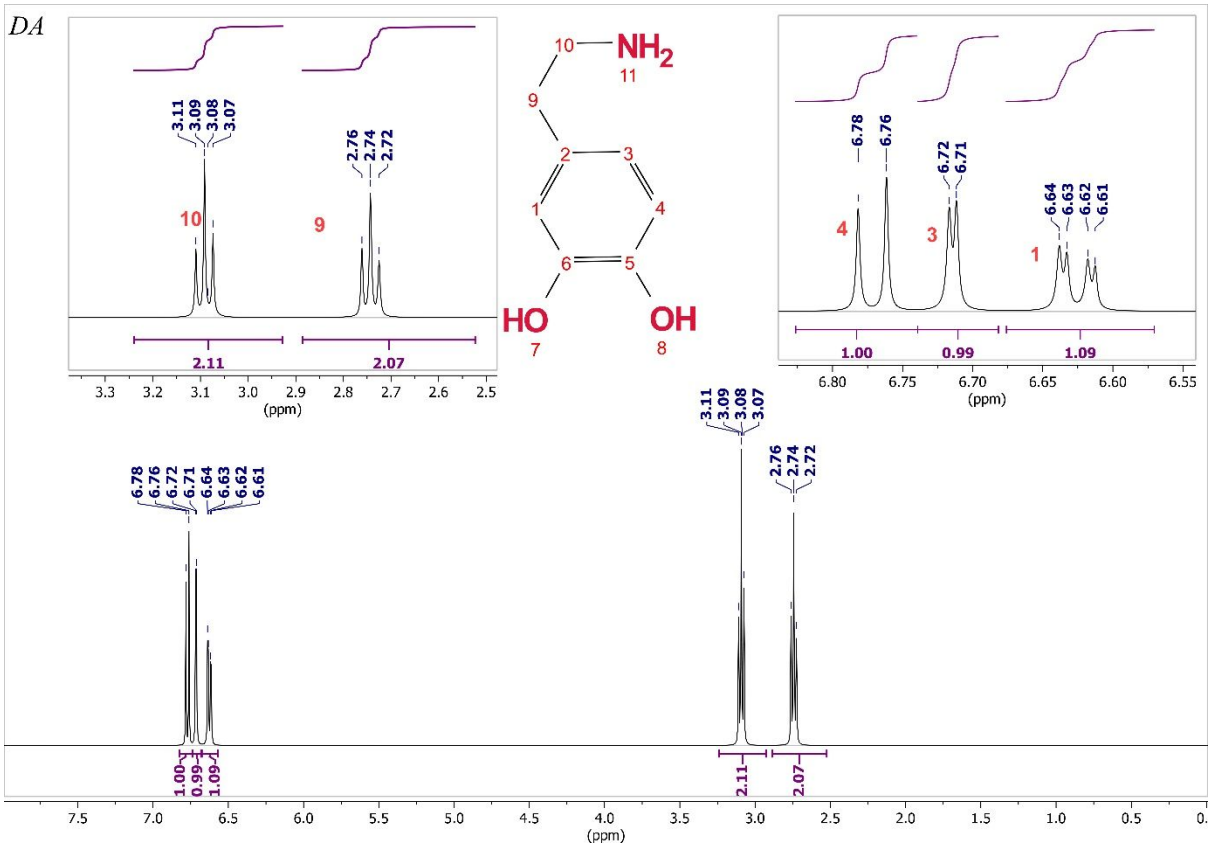

Figure S5. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) 1 mM dopamine (DA) in deuterium oxide (D_2O).

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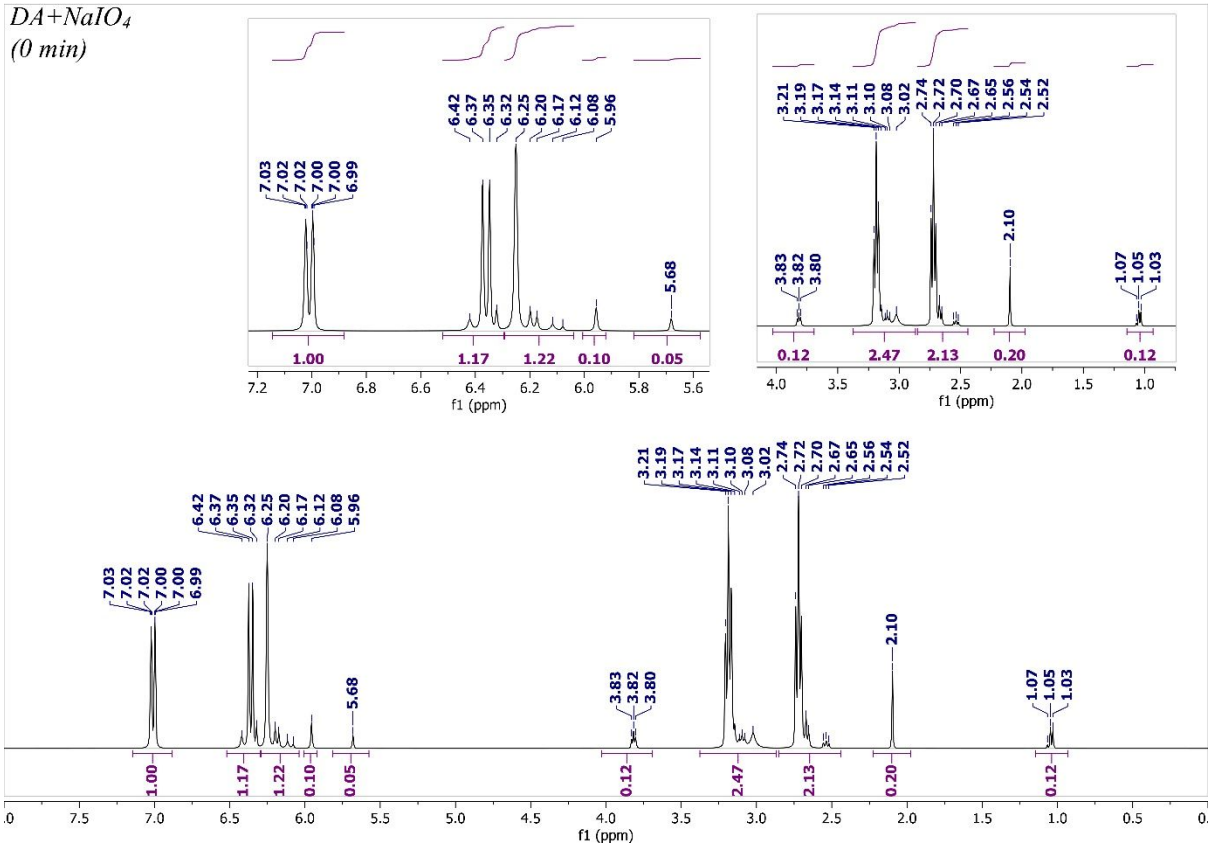

Figure S6. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for dopamine (DA) in deuterium oxide (D_2O) immediately after the addition of 1 mM $NaIO_4$ at 0 min.

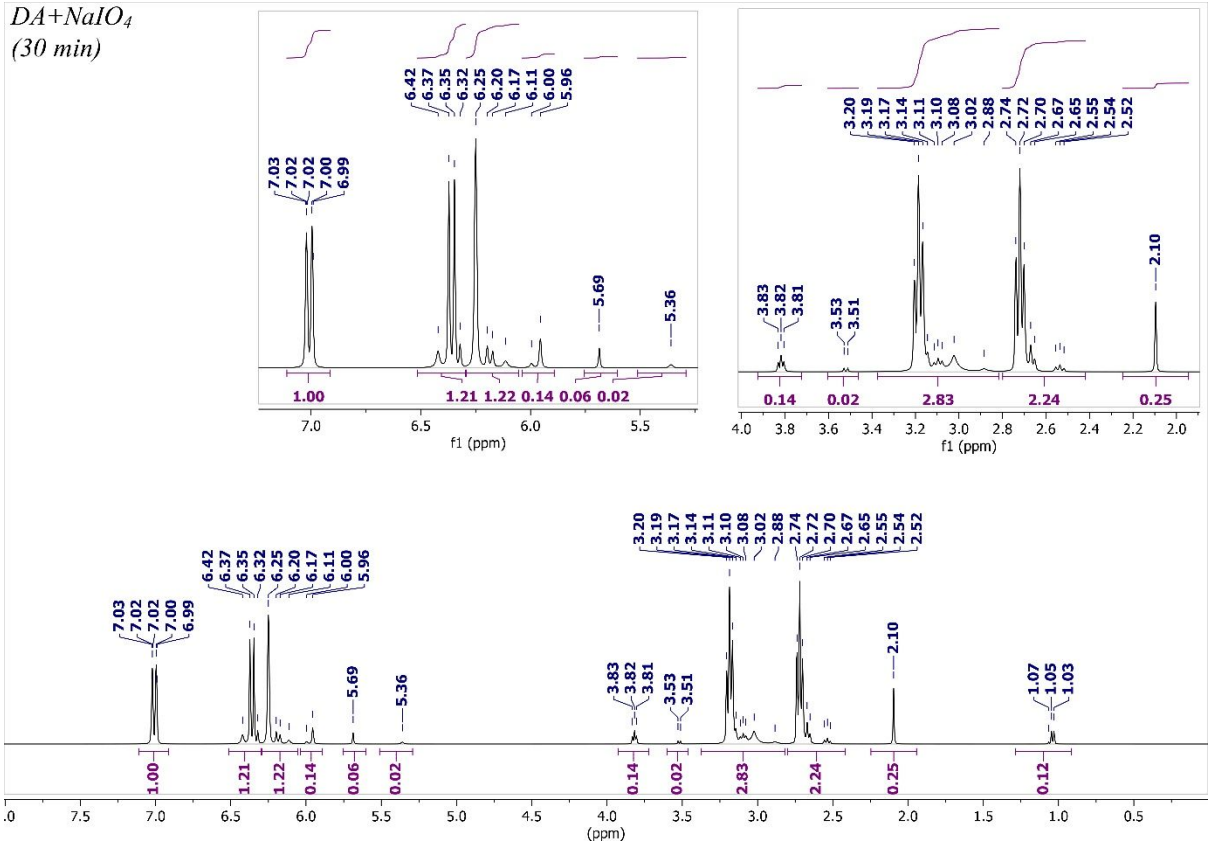

Figure S7. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for dopamine (DA) in deuterium oxide (D_2O), 30 min after addition of 1 mM $NaIO_4$.

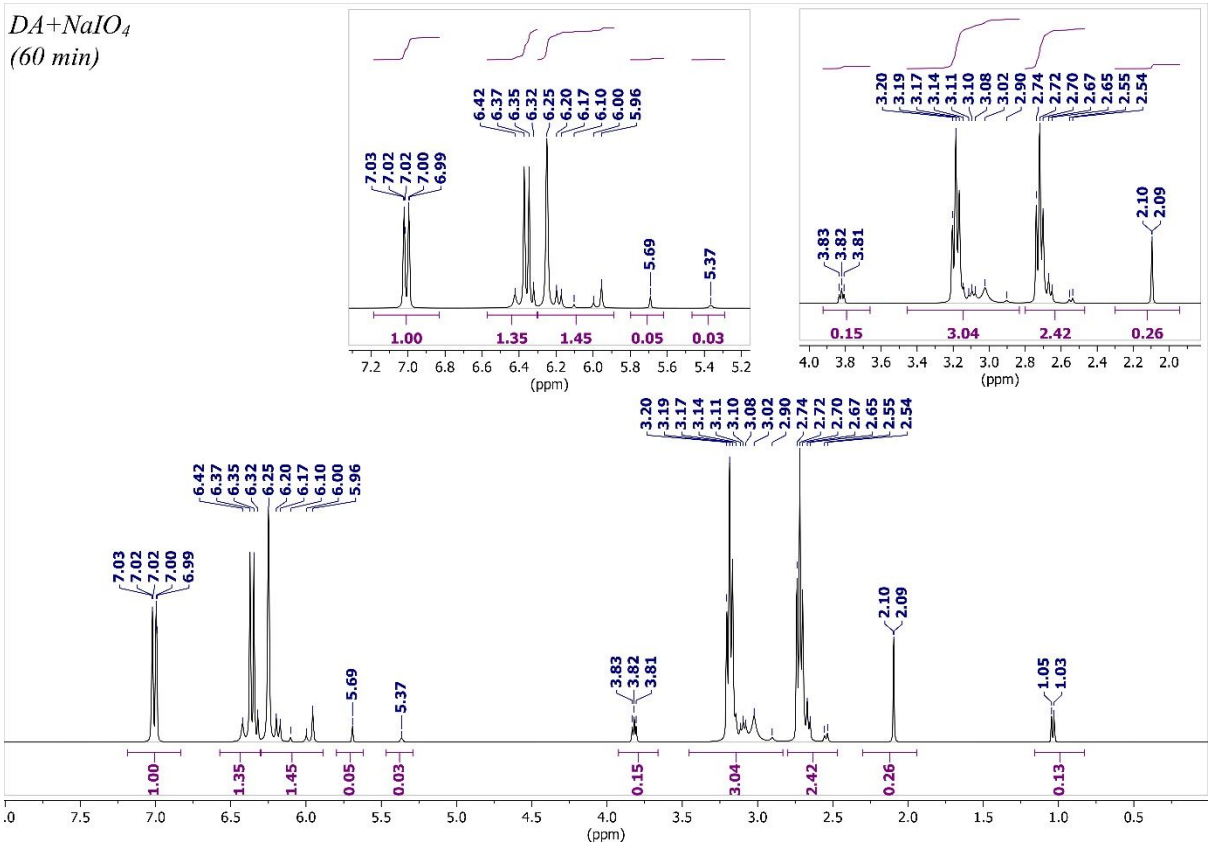

Figure S8. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for dopamine (DA) in deuterium oxide (D_2O), 60 min after addition of 1 mM $NaIO_4$.

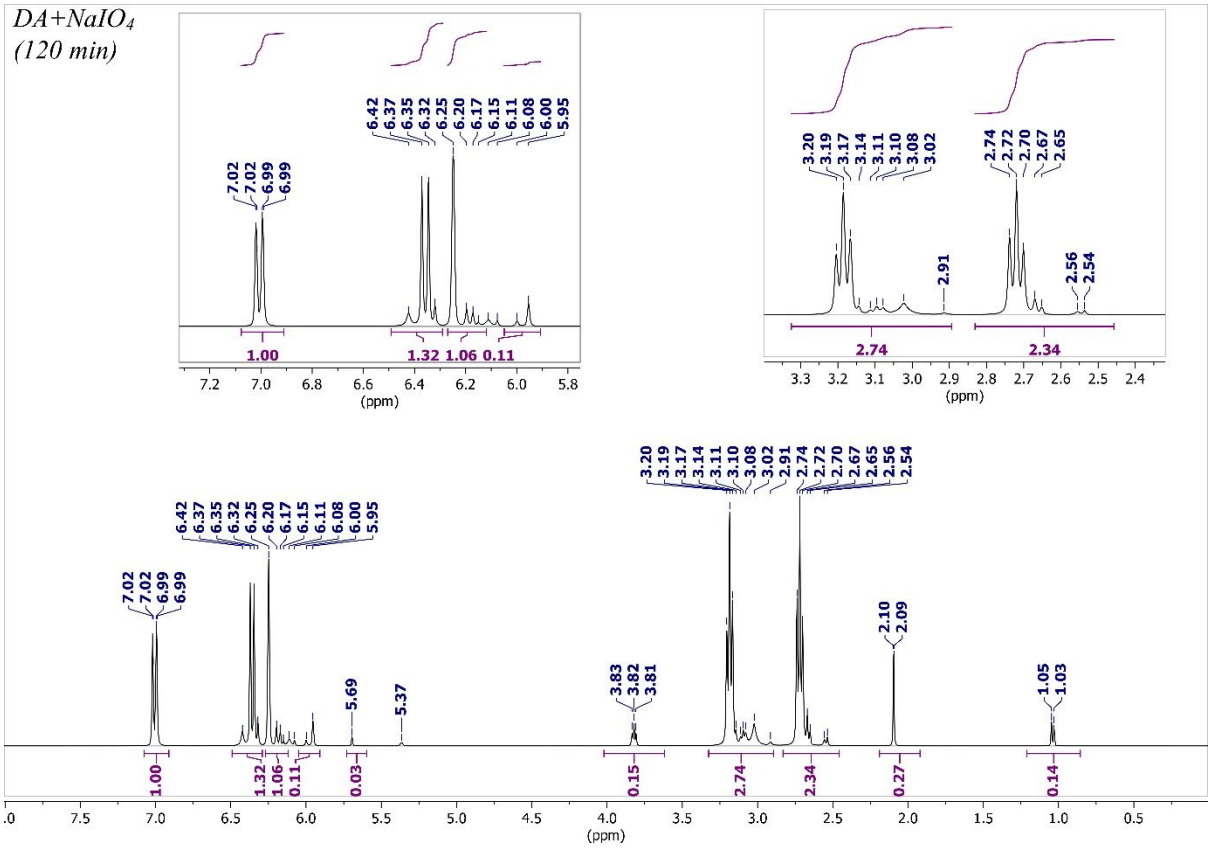

Figure S9. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for dopamine (DA) in Deuterium oxide (D_2O), 120 min after addition of 1 mM $NaIO_4$.

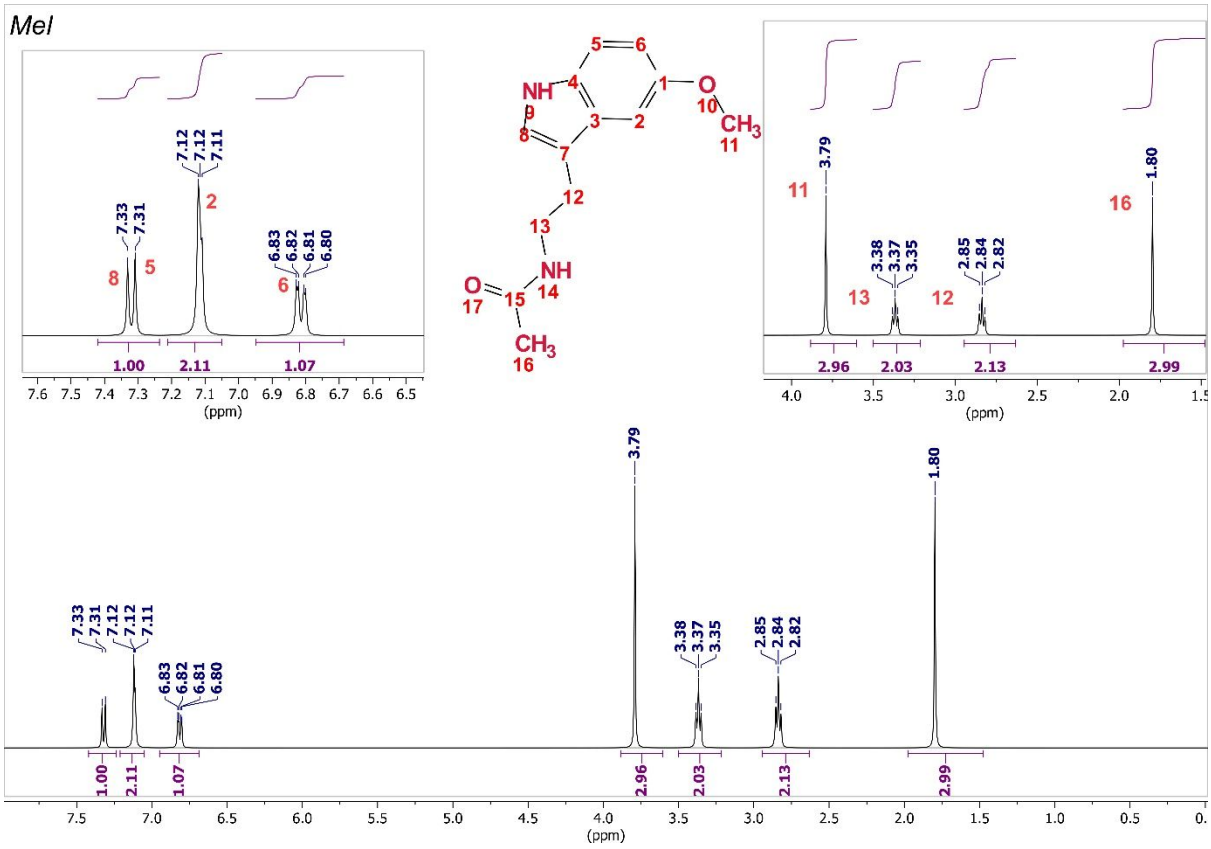

Figure S10. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for 1 mM melatonin (Mel) dissolved in Deuterium oxide (D_2O) and dimethyl sulphoxide (DMSO) solvent mixture.

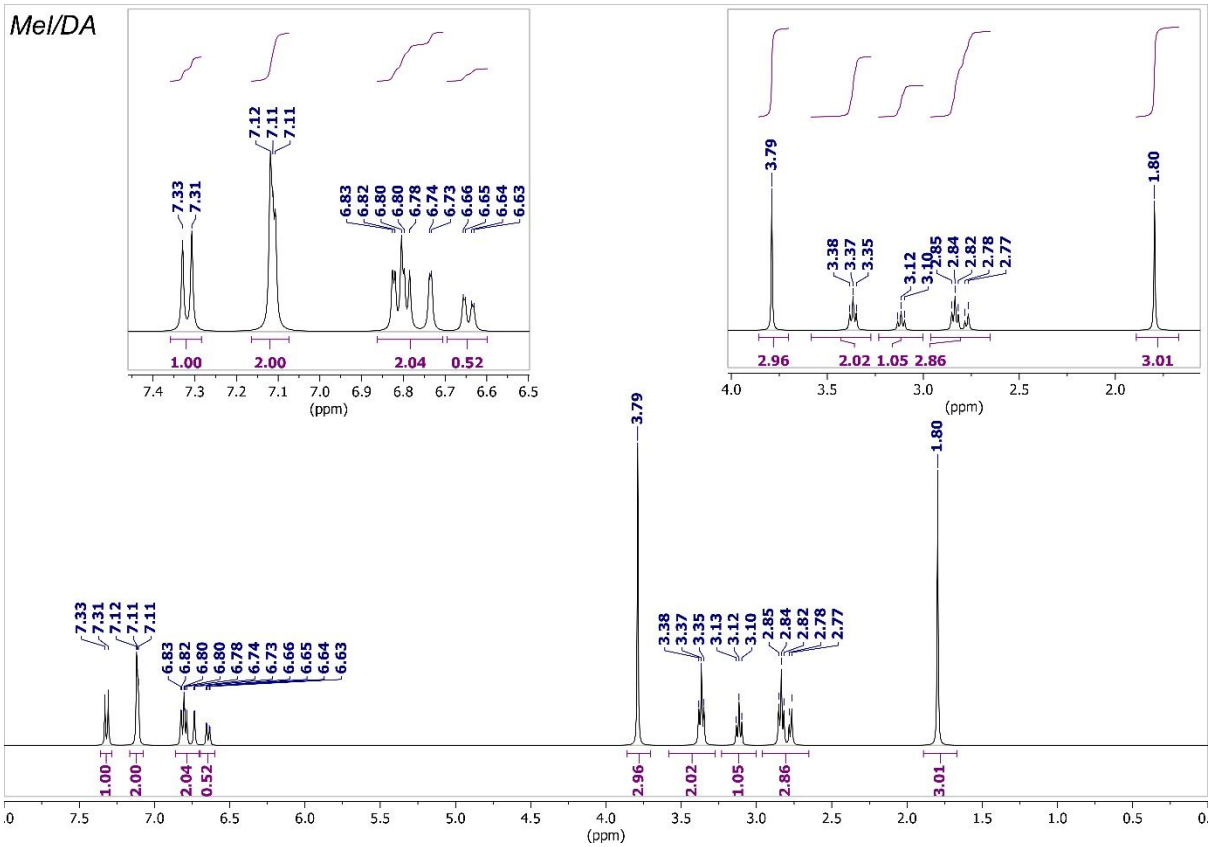

Figure S11. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for 1mM melatonin (Mel) with 1 mM dopamine (DA) in Deuterium oxide (D_2O) and dimethyl sulphoxide (DMSO) solvent mixture.

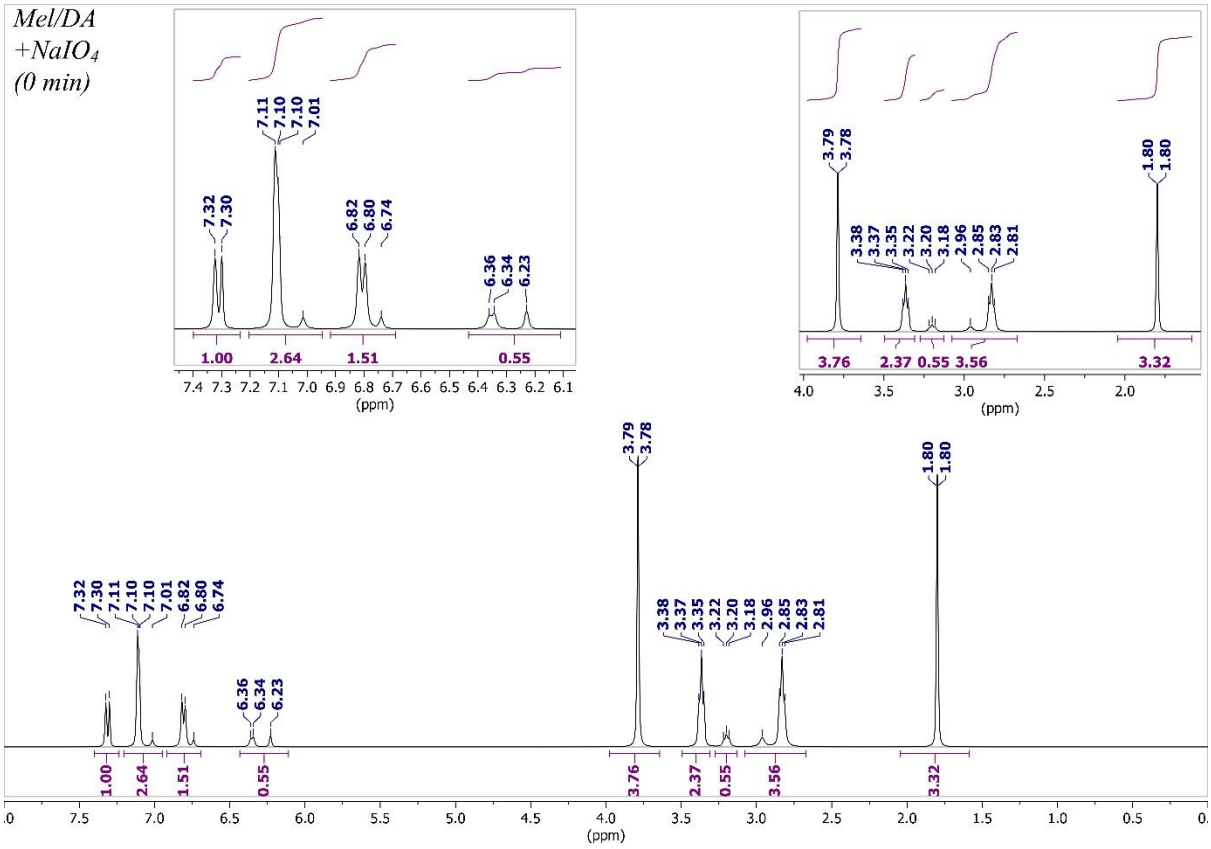

Figure S12. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for 1 mM melatonin (Mel) with 1 mM dopamine (DA) immediately after adding (0 min) 1mM $NaIO_4$ in Deuterium oxide (D_2O) and dimethyl sulphoxide (DMSO) solvent mixture.

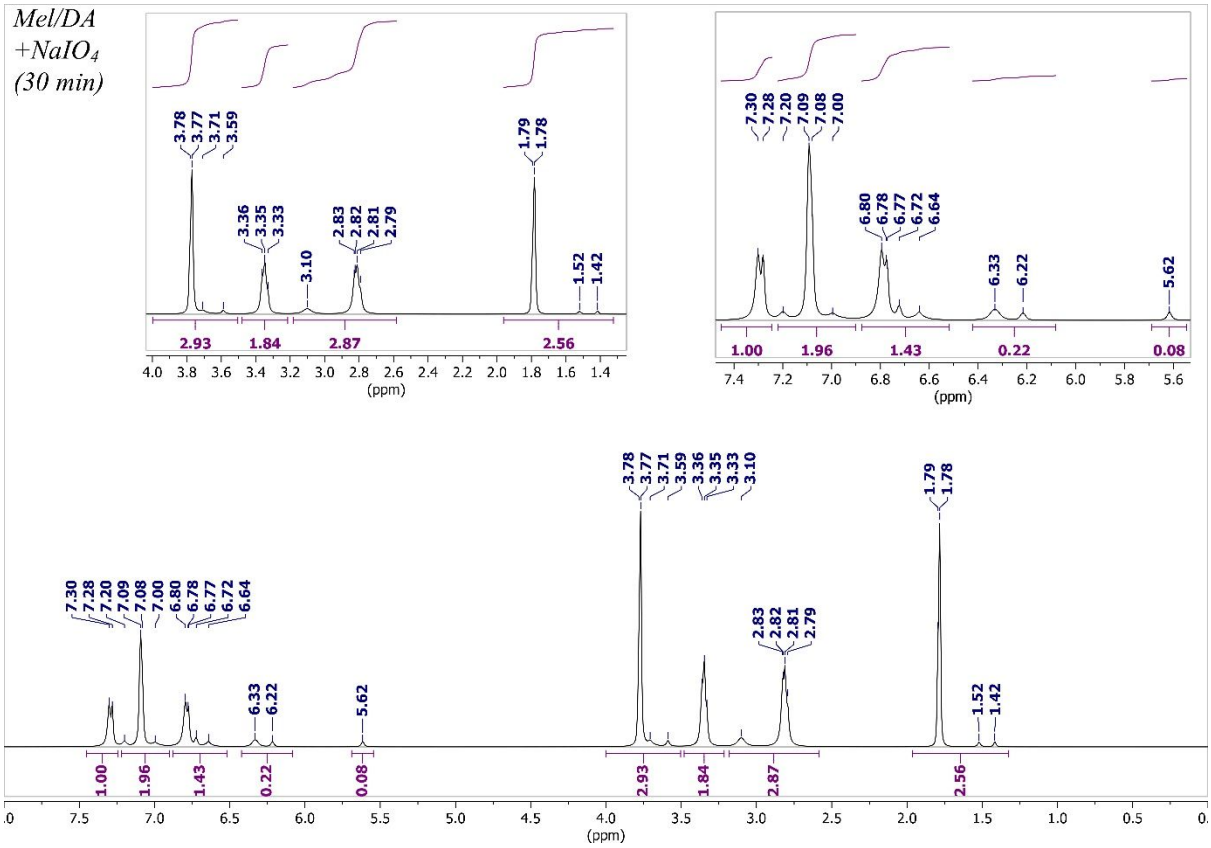

Figure S13. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for 1 mM melatonin (Mel) with 1 mM dopamine (DA), 30 min after addition of 1mM $NaIO_4$ in Deuterium oxide (D_2O) and dimethyl sulphoxide (DMSO) solvent mixture.

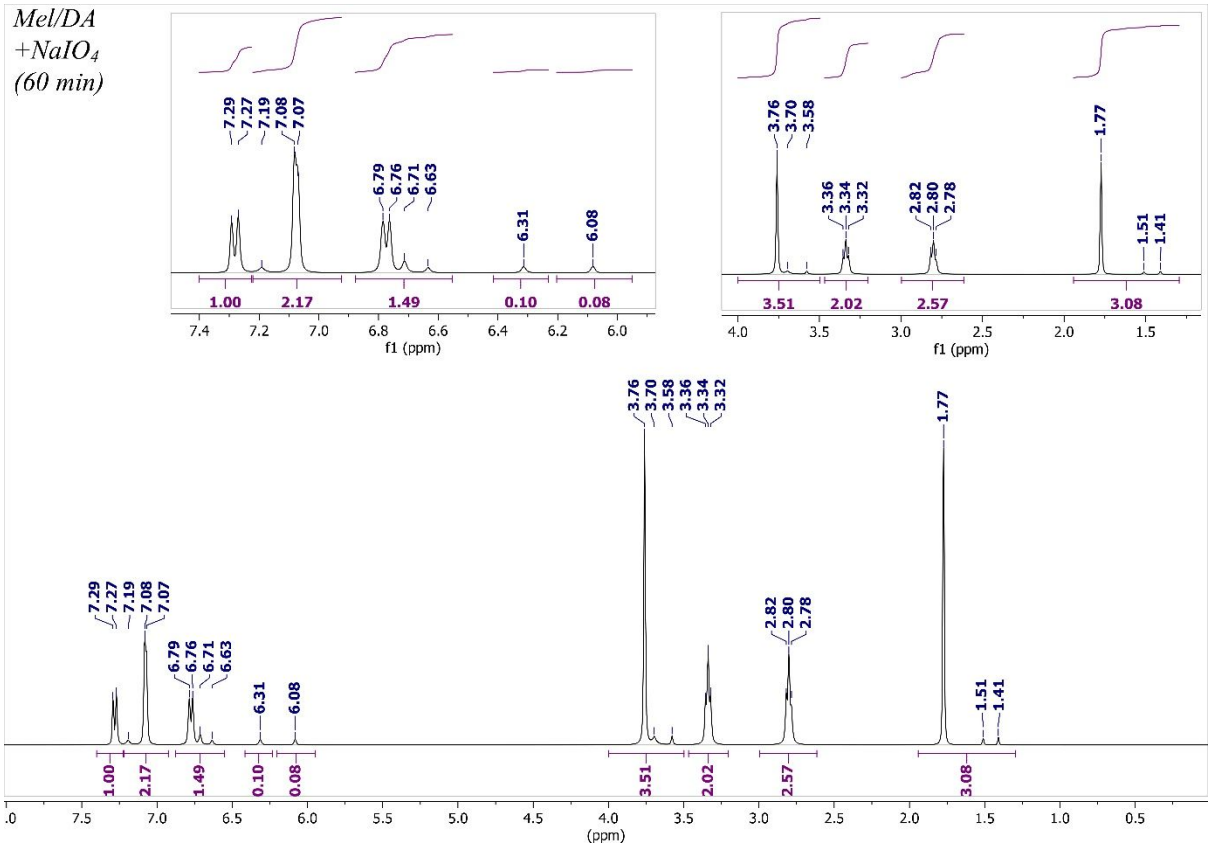

Figure S14. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for 1 mM melatonin (Mel) with 1 mM dopamine (DA), 60 min after addition of 1mM $NaIO_4$ in Deuterium oxide (D_2O) and dimethyl sulphoxide (DMSO) solvent mixture.

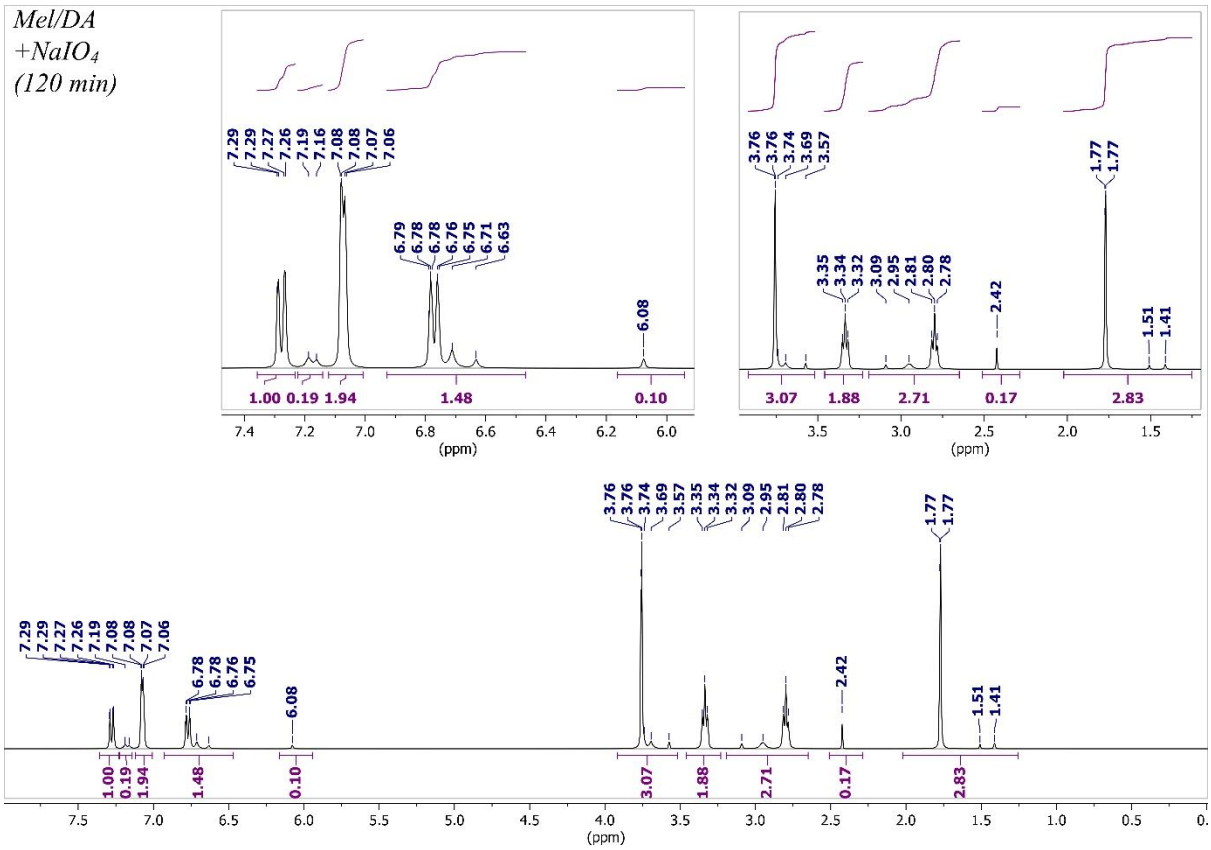

Figure S15. The 1H NMR spectrum acquired (0 ppm to 8 ppm, right to left) for 1 mM melatonin (Mel) with 1 mM dopamine (DA), 120 min after addition of 1mM $NaIO_4$ in Deuterium oxide (D_2O) and dimethyl sulphoxide (DMSO) solvent mixture.

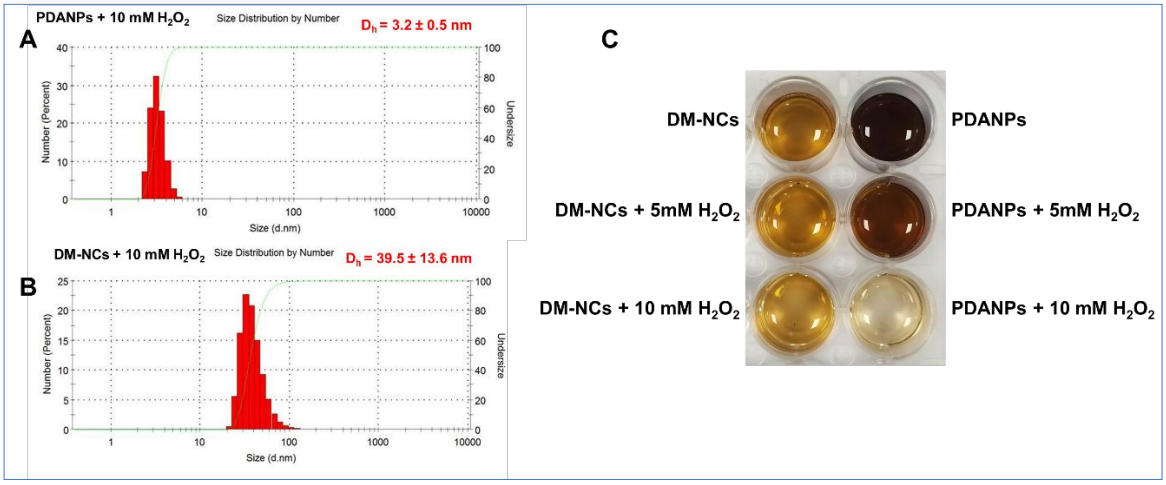

Figure S16. Stability of DM-NCs against H_2O_2. Mean particle size distribution of (A) PDANPs, (B) DM-NCs in H_2O_2 solution. (C) The progressive fading of the black color of PDANPs upon H_2O_2 addition but no color change observed in DM-NCs dispersion.

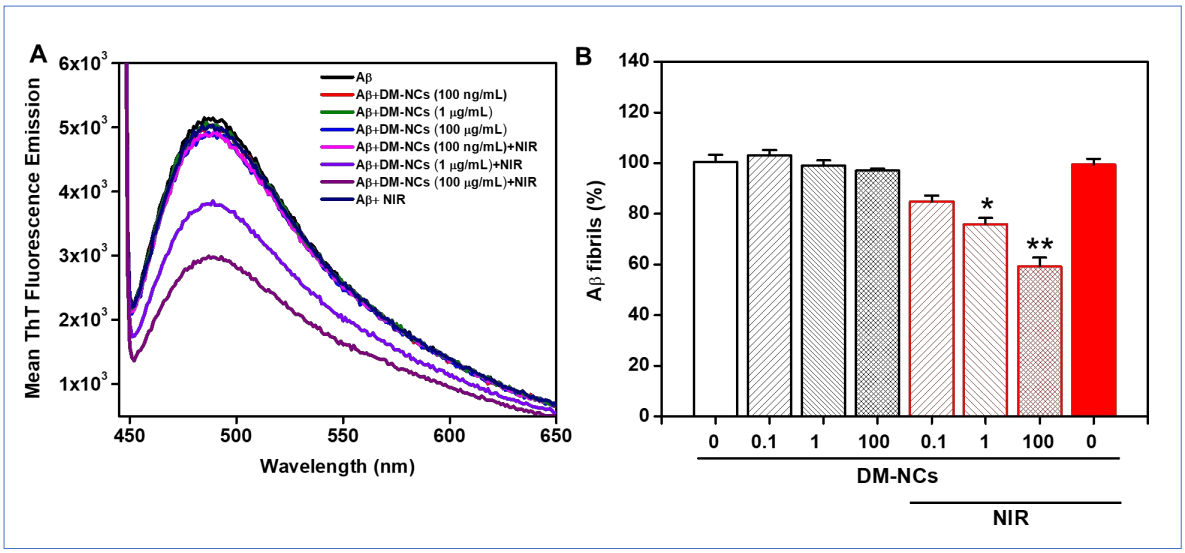

Figure S17. A*β* disaggregation by DM-NCs examined using, (A) ThT fluorescence emission spectrum for native A*β* fibrils, A*β* fibrils incubated with DM-NCs and A*β* fibrils incubated with DM-NCs with NIR illumination. (B) A*β* fibrils (%) (mean ± SD) represented as a bar diagram.

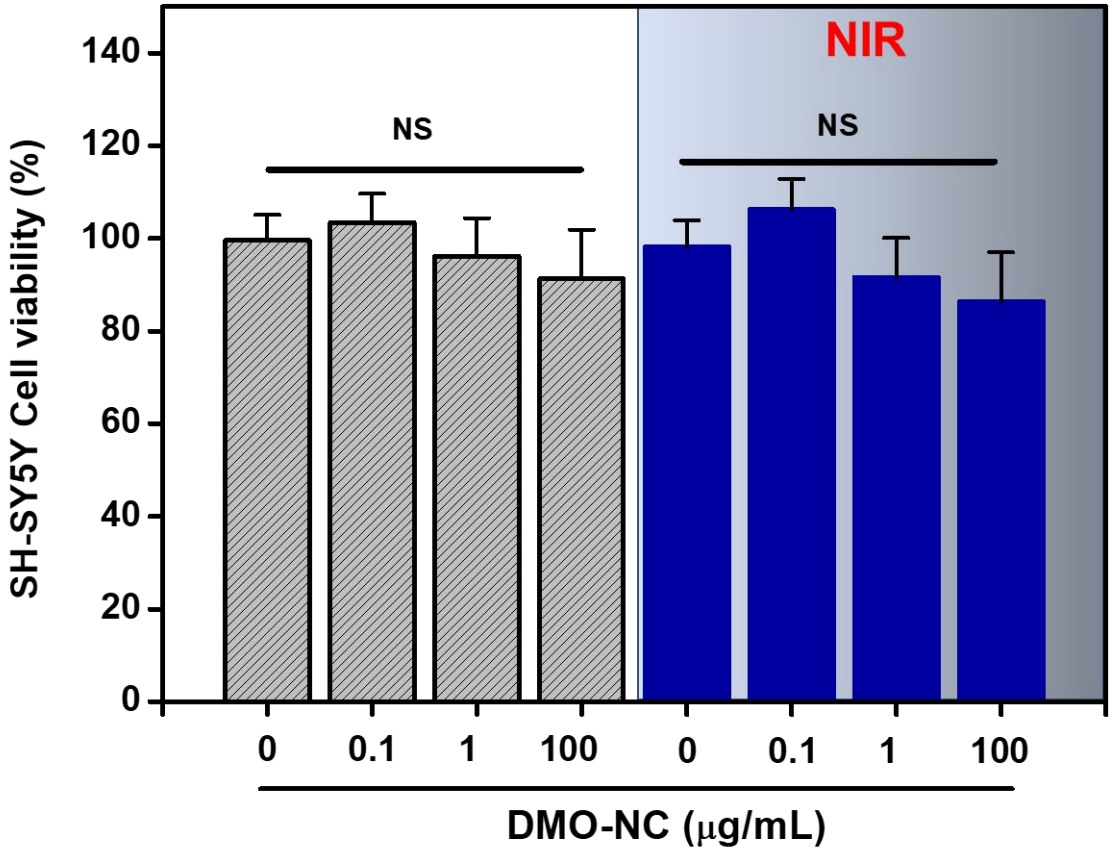

Figure S18. The SH-SY5Y cell viability measured using MTT assay following exposure with DM-NCs (100 ng/mL, 1 μg/mL, and 100 μg/mL) and DM-NCs with NIR.