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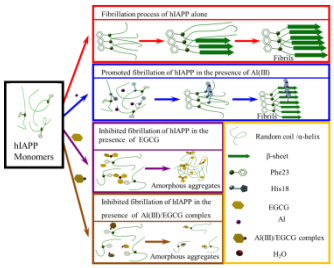

hIAPP monomers self-assemble into fibrils. EGCG efficiently inhibits this process, and even can inhibit Al(III)-induced fibrillation via Al(III)/EGCG complex of $Al(EGCG)(H_2O)_2$.

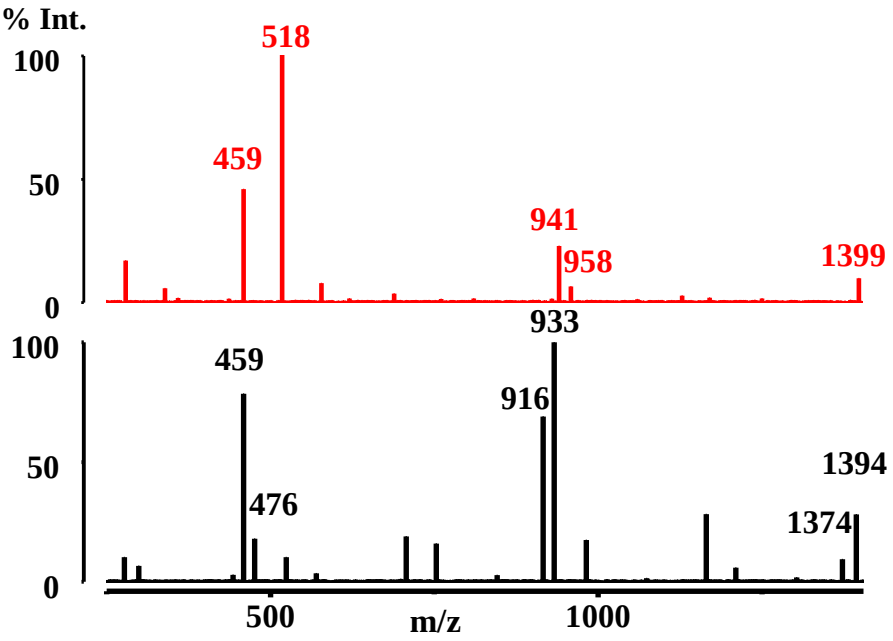

Fig. S1 ESI mass spectra of 10 mM EGCG without (bottom) and with (top) 10 mM Al(III).

Table S1 Assignments of ESI mass spectra of EGCG and Al(III)/EGCG complex[a]

EGCG		Al(III)/EGCG	
m/z	ion	m/z	ion
459	H^+E	459	H^+E
476	H^+EW	518	$Al^{3+}(H^+)_{-2}EW_2$
916	H^+E_2	941	$Al^{3+}(H^+)_{-2}E$
933	H^+E_2W	958	$Al^{3+}(H^+)_{-2}E_2W$
1374	H^+E_3	1399	$Al^{3+}(H^+)_{-2}E_3$
1394	Na^+E_3		

[a]E and W represent EGCG and water, respectively.

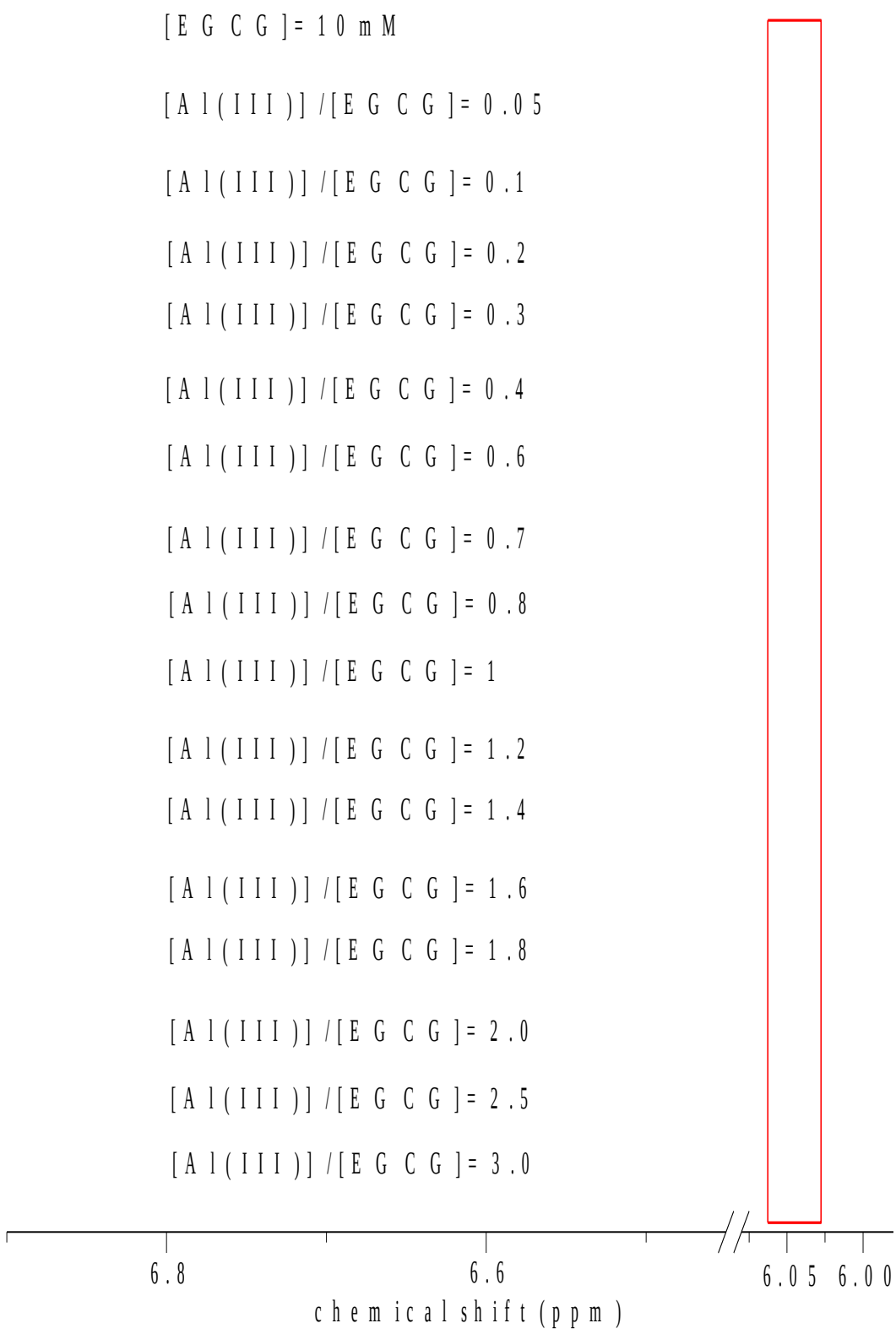

Fig. S2 ^{1}H NMR spectra of 10 mM EGCG in the presence of Al(III) at various concentrations from 0 to 30 mM. Intensity of peak at 6.04 ppm decreased with the titration of Al(III)

Table S2 Assignments of ^{1}H NMR spectra of EGCG and Al(III)/EGCG complex

EGCG		Al(III)/EGCG	
δ (ppm)	sites	δ (ppm)	sites
6.92	H-3'' and H-7''	6.92	H-3'' and H-7''
6.50	H-2' and H-6'	6.80	H-3'' and H-7''
6.04	H-9	6.75	H-3'' and H-7''
6.02	H-7	6.55	H-2' and H-6'
2.77-2.95	H-4	6.50	H-2' and H-6'
		6.04	H-9
		6.02	H-7
		2.77-2.95	H-4

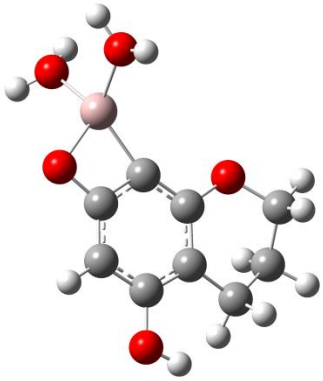

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Fig. S3 Geometries and Cartesian coordinates of AE-1. Red, gray, pink and white balls represent oxygen, carbon, aluminum and hydrogen atoms respectively.

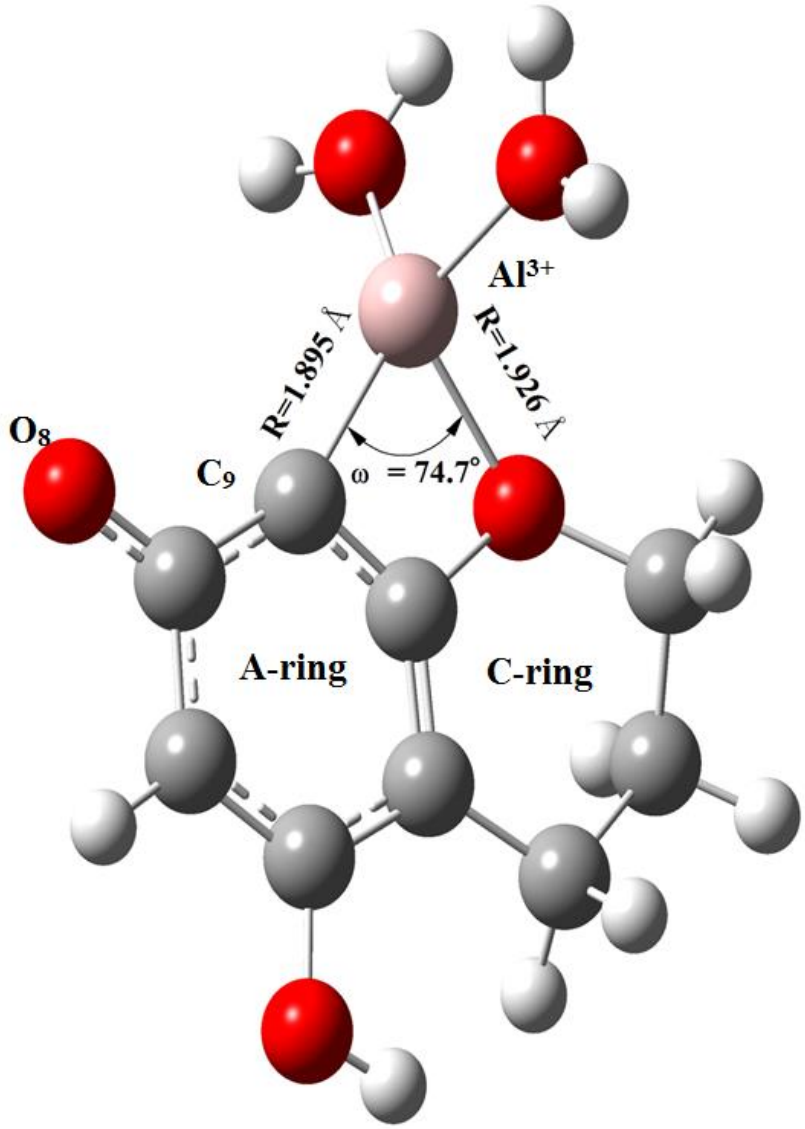

Fig. S4 Illustration of Al(EGCG)$(H_2O)_2$ complex 2 (AE-2). Red, gray, pink and white balls represent oxygen, carbon, aluminum and hydrogen atoms respectively. C_9 in A-ring and O atom in C-ring of EGCG form coordination bonds with aluminum.

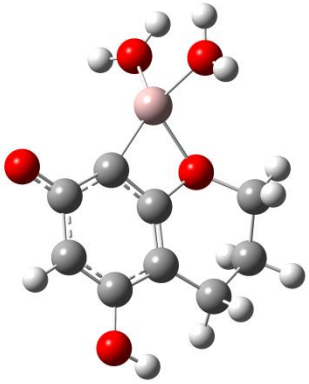

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Fig. S5 Geometries and Cartesian coordinates of AE-2. Red, gray, pink and white balls represent oxygen, carbon, aluminum and hydrogen atoms respectively.

Table S3 Binding free energies and their components from quantum chemical calculations for Al(III)/EGCG complexes (a.u.)

Contributions	AE-1	AE-2
$G_{(complex)}$	-968.27	-968.23
$G_{(H^+)}$	-0.23	-0.23
$G_{(Al^{3+})}$	-241.40	-241.40
$G_{(EGCG \bullet H_{-1})}$	-573.86	-573.86
$G_{(H_2O)}$	-76.41	-76.41
$\Delta G_{binding}$	-0.43	-0.39

Table S4 Fibrillation kinetic parameters of hIAPP on Al(III) concentration by ThT fluorescence assay

[Al] (μM)	I_{max}(A.U.)	$t_{1/2}$(min)	k(min^{-1})	t_0(min)	R
0	211.5±1.3	20.8±0.2	0.278±0.016	13.6±0.5	0.985
2	186.1±1.1	17.2±0.2	0.274±0.015	9.9±0.5	0.984
8	180.5±0.6	16.4±0.1	0.239±0.006	8.0±0.3	0.997
64	197.4±0.9	14.0±0.2	0.199±0.007	4.0±0.4	0.987

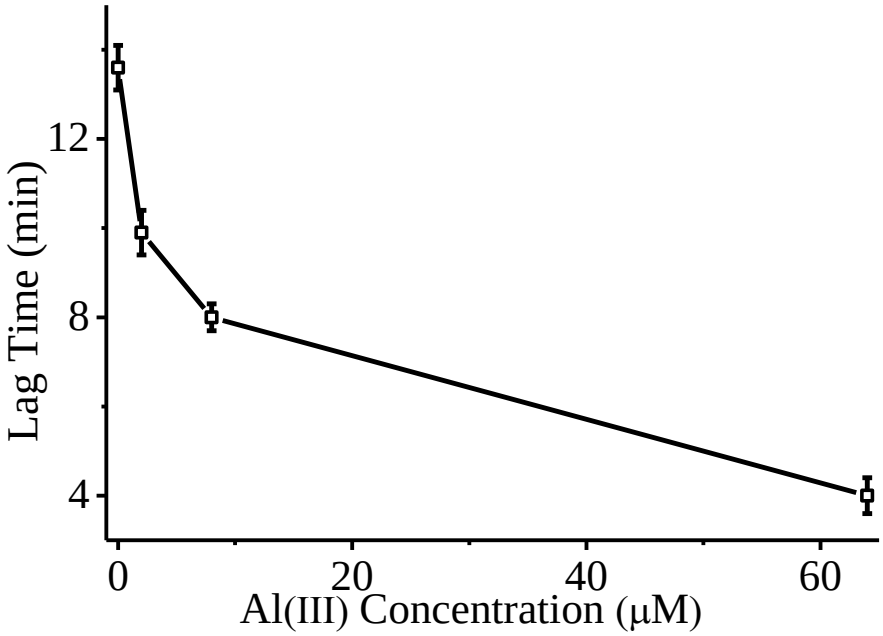

Fig. S6 Lag time (t_0) of 16 μM hIAPP fibrillation on Al(III) concentration

Table S5 Aggregation kinetic parameters of hIAPP with and without Al(III) by ^{1}H NMR

[Al] (μM)	I_{max}	$t_{1/2}$(min)	k(min^{-1})	t_0(min)	R
0	0.98±0.01	87.3±0.7	0.106±0.007	69±1	0.992
12.5	0.93±0.02	84.0±1.1	0.114±0.012	66±2	0.983

Table S6 Assignments of ^{1}H NMR spectra of aromatic resonances of hIAPP

δ (ppm)	residues	sites
7.24-7.28	Phe15/23	Hε
7.21-7.24	Phe15/23	Hδ
7.17-7.21	His18	Hδ
7.11-7.17	Phe15/23	Hζ
7.00-7.02	Tyr37	Hε
6.71-6.73	Tyr37	Hδ

Table S7 Fibrillation kinetic parameters of hIAPP on EGCG concentration by ThT fluorescence assay

[EGCG] (μM)	I_{max}(A.U.)	$t_{1/2}$(min)	k(min^{-1})	t_0(min)	R
0	186.9±3.1	23.0±0.9	0.122±0.004	6.6±1.8	0.983
2	136.0±3.0	39.6±1.1	0.069±0.004	10.5±2.0	0.995
8	101.0±0.9	38.4±0.4	0.102±0.003	18.7±0.8	0.995
16	69.8±0.5	35.3±0.4	0.113±0.004	17.6±0.7	0.986
32	42.2±0.4	23.4±0.4	0.169±0.010	11.6±0.8	0.986

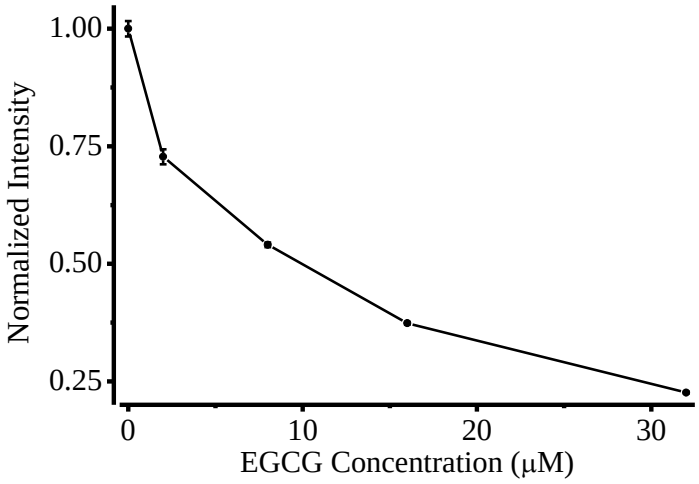

Fig. S7 The maximum ThT fluorescence intensity (I_{max}) of 16 μM hIAPP on EGCG concentration. The intensity values were normalized to the hIAPP alone data.

Table S8 Aggregation kinetic parameters of hIAPP with and without EGCG by ^{1}H NMR

[EGCG] (μM)	I_{max}	$t_{1/2}$(min)	k(min^{-1})	t_0(min)
0	0.98±0.01	87.3±0.7	0.106±0.007	69±1
12.5	1.06±0.01	113.2±1.1	0.051±0.003	74±2

Table S9 ^{1}H NMR peak line width at half maximum height ($W_{1/2}$) of EGCG on molar ratio of [hIAPP]/[EGCG]

[hIAPP]/[EGCG]	$W_{1/2}$ (Hz)	
	6.92 ppm	6.50 ppm
0	0.6	1.28
0.02	1.48	1.88
0.1	2.26	2.6

Table S10 Fibrillation kinetic parameters of 16 μM hIAPP with 2 μM EGCG on Al(III) concentration by ThT fluorescence assay

[Al] (μM)	I_{max}(A.U.)	$t_{1/2}$(min)	k(min^{-1})	t_0(min)
0	106.1±0.6	52.9±0.3	0.100±0.002	32.9±0.6
1	102.9±0.6	69.3±0.3	0.092±0.002	47.7±0.5
2	97.6±0.8	70.3±0.4	0.082±0.002	45.9±0.7
4	116.6±0.8	62.3±0.4	0.092±0.002	40.5±0.7
16	117.5±0.7	44.4±0.3	0.114±0.004	26.9±0.7
64	129.4±0.5	31.9±0.2	0.156±0.004	19.1±0.4

Table S11 Nucleation kinetic parameters of hIAPP by DLS assay

hIAPP co-incubated compounds	D_0(nm)	k	n
-	34.9±8.5	9.4±0.7	1.56±0.15
2 μM EGCG	12.8±4.4	31.9±1.4	1.11±0.06
2 μM Al(III)	18.8±7.2	19.5±0.8	1.44±0.08
2 μM Al(III)/EGCG (1:1)	20.2±7.5	43.8±2.0	1.17±0.05