

Supplemental materials

Table S1. Chemicals and their sources.

Chemicals	Source	Catalog number	Address
Curcumin	Sigma	C1386-50G	St. Louis, MO
Bisdemethoxycurcumin	Sigma	B6938-25MG	St. Louis, MO
Demethoxycurcumin	Sigma	D7696-25MG	St. Louis, MO
Tetrahydrocurcumin	Sigma	SMB00370-1G	St. Louis, MO
Hexafluoroisopropanol	Sigma	8045150025	St. Louis, MO
A β 42	Sigma	A9810-.1MG	St. Louis, MO
6E10	BioLegend	803001	San Diego, CA
A11	Thermo Fisher Scientific	AHB0052	Waltham, MA
OC	Millipore-Sigma	AB2286	Burlington, MA
Caspase-3	Cell Signaling Technology	14220	Danvers, MA
Chemiluminescent kit	ThermoScientific	34096	Waltham, MA
Silver stain kit	Thermo Fisher Scientific	24612	Waltham, MA
N2A cells	ATCC	ATCC® CCL-131	Manassas, VA
SH-SY5Y cells	ATCC	ATCC®CRL-2266	Manassas, VA
Eagle's Minimum Essential Media	GIBCO	ATCC	Manassas, VA
DMEM: F12K	GIBCO	11320-033	Manassas, VA
Fetal bovine serum	GIBCO	A4766801	Manassas, VA
MTT	Sigma	M2128-5G	St. Louis, MO
96-well plates	Denville Scientific Inc	2019001	Metuchen, NJ
Ammonium persulphate	Fisher Scientific	BP179-25	Waltham, MA
RuBpy	Sigma	754730	St. Louis, MO
PVDF membrane	Millipore	IPVH00010	Bedford, MA
β -mercaptoethanol	GIBCO	21985	Manassas, VA
Copper grid	Sigma	G4901-1VL	St. Louis, MO
Glutaraldehyde	Sigma	G5882	St. Louis, MO
BCA kit	Thermo Fisher Scientific	BCA1-1KT	Waltham, MA

Table S2. Different chemicals and their amounts used in PICUP reaction. APS: ammonium per sulphate; RuBpy: ruthenium bipyridine.

A β 42 (μ L)	APS (μ L)	RuBpy (μ L)	Light exposure (μ L)	β -mercaptoethanol
18	1	1	1	10
38	2	2	1	20

Table S3. Binding affinity levels in Cur derivatives when interacting with A β 40 and A β 42. The binding affinity were calculated using Auto Dock Vina software. Note that the keto and enol form of curcumin were more likely interacted both A β 40 and 42. Also, the more bioavailable THC has stronger binding affinity for the A β 42 over A β 40.

Derivatives	Interactions with amino acids of A β 40	Binding affinity(kcal/mol)	Interactions with amino acids of A β 42	Binding affinity (kcal/mol)
KCur	Asp-1, Gly-9, Tyr-10, Lys-16, Leu-17, Phe-20	-6.3	Glu-3, His-6, Tyr-10, His-13	-5.5
ECur	Glu-3, His-6, Tyr-10, His-13, His-14	-6.1	Glu-3, His-6, Tyr-10, His-14	-5.4
BDMC	Asp-1, Glu-3, Val-12, His-13, Lys-16, Phe-20	-5.9	His-6, Tyr-10	-5.2
DMC	Glu-3, Gly-9, Val-12, His-13, Lys-16	-5.5	Ser-8, Val-12, Lys-16, Phe-19	-5
THC	Asp-1, Glu-3, Lys-16, Phe-20	-4.8	Glu-3, His-6, Asp-7, Tyr-10, His-13, His-14	-5

Table S4. Hydrogen bond formation of different amino acids of A β 40 and A β 42 when interacted with KCur and THC.

A β -40-Kcur			A β -40-THC Simulation		
Found	20	H-bonds	Found	28	H-bonds.
Donor	Acceptor	Occupancy	Donor	Acceptor	Occupancy
LIG1-Side	ASP7-Main	0.01%	ASP1-Main	LIG1-Side	0.36%
LIG1-Side	ASP1-Main	0.29%	LIG1-Side	ASP7-Main	0.02%
LIG1-Side	GLU3-Side	0.01%	HSD6-Main	LIG1-Side	0.20%
HSD13-Side	LIG1-Side	0.07%	LIG1-Side	PHE4-Main	0.01%
LIG1-Side	ALA2-Main	0.07%	LYS16-Side	LIG1-Side	0.29%
ASN27-Side	LIG1-Side	0.26%	SER8-Side	LIG1-Side	0.05%
LYS16-Side	LIG1-Side	0.22%	ALA2-Main	LIG1-Side	0.05%
LIG1-Side	VAL24-Main	0.10%	GLY9-Main	LIG1-Side	0.13%
LYS28-Side	LIG1-Side	0.49%	TYR10-Side	LIG1-Side	0.10%
LIG1-Side	ASN27-Side	0.02%	LIG1-Side	GLY9-Main	0.04%
TYR10-Side	LIG1-Side	0.49%	SER8-Main	LIG1-Side	0.11%
PHE4-Main	LIG1-Side	0.65%	LIG1-Side	ASP7-Side	0.20%

LIG1-Side	HSD6-Side	0.04%	LIG1-Side	ASP23-Side	0.36%
LIG1-Side	ALA21-Main	0.06%	LIG1-Side	TYR10-Side	0.02%
LIG1-Side	GLU22-Side	0.12%	ASN27-Side	LIG1-Side	0.04%
LIG1-Side	TYR10-Main	0.01%	LIG1-Side	ASN27-Side	0.01%
SER26-Side	LIG1-Side	0.04%	LIG1-Side	SER8-Side	0.12%
ASP1-Main	LIG1-Side	0.01%	LIG1-Side	GLU11-Side	0.25%
TYR10-Main	LIG1-Side	0.04%	LIG1-Side	HSD14-Side	0.05%
GLY9-Main	LIG1-Side	0.01%	LIG1-Side	GLU3-Main	0.18%
			ARG5-Side	LIG1-Side	0.06%
			ARG5-Main	LIG1-Side	0.10%
			TYR10-Main	LIG1-Side	0.22%
			GLU11-Main	LIG1-Side	0.10%
			ASP7-Main	LIG1-Side	0.17%
			LIG1-Side	LYS16-Main	0.36%
			LIG1-Side	GLN15-Main	0.04%
			LYS16-Main	LIG1-Side	0.67%
Aβ-42-KCur Simulation			Aβ-42-THC Simulation		
Found	19	H-bonds	Found	25	H-bonds.
Donor	Acceptor	Occupancy	Donor	Acceptor	Occupancy
LIG1-Side	GLU3-Side	0.06%	HSD6-Side	LIG1-Side	0.11%
ASP1-Main	LIG1-Side	0.05%	LIG1-Side	HSD14-Side	0.05%
LIG1-Side	GLN15-Side	0.26%	LIG1-Side	GLU3-Side	0.05%
LIG1-Side	GLU11-Side	0.01%	LIG1-Side	TYR10-Main	0.01%
GLN15-Side	LIG1-Side	0.02%	HSD14-Side	LIG1-Side	0.44%
HSD6-Side	LIG1-Side	0.06%	LIG1-Side	LEU17-Main	0.01%
LIG1-Side	ALA21-Main	0.01%	LIG1-Side	ASP1-Side	0.13%
LIG1-Side	HSD6-Main	0.01%	TYR10-Side	LIG1-Side	0.01%

LIG1-Side	ILE41-Main	0.10%	LIG1-Side	HSD13-Side	0.10%
LIG1-Side	ASP7-Side	0.02%	LIG1-Side	SER8-Side	0.01%
LIG1-Side	VAL40-Main	0.09%	LIG1-Side	VAL36-Main	0.01%
LIG1-Side	VAL39-Main	0.17%	LIG1-Side	ASP1-Main	0.04%
HSD6-Main	LIG1-Side	0.01%	ALA30-Main	LIG1-Side	0.04%
LIG1-Side	LYS28-Main	0.02%	ASN27-Side	LIG1-Side	0.07%
ARG5-Side	LIG1-Side	0.11%	LIG1-Side	ASN27-Side	0.12%
TYR10-Side	LIG1-Side	0.03%	LYS28-Main	LIG1-Side	0.05%
LIG1-Side	ALA42-Side	0.78%	LIG1-Side	SER26-Main	0.02%
ALA42-Main	LIG1-Side	0.14%	LYS16-Side	LIG1-Side	0.30%
TYR10-Main	LIG1-Side	0.02%	LIG1-Side	GLU22-Side	0.32%
			LIG1-Side	ALA42-Side	0.01%
			ILE31-Main	LIG1-Side	0.04%
			LIG1-Side	HSD6-Side	0.01%
			ARG5-Side	LIG1-Side	0.28%
			LIG1-Side	HSD6-Main	0.06%
			LIG1-Side	VAL40-Main	0.01%

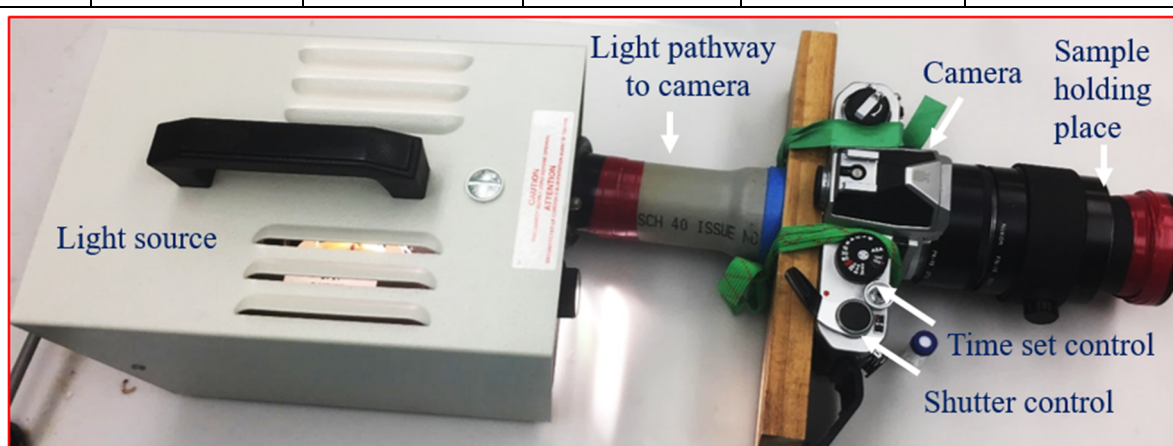


Figure S1. Camera apparatus used to irradiate the protein mixture to perform photo-induced cross-linking of unmodified protein (PICUP). It includes a light source and a camera with shutter and time control.

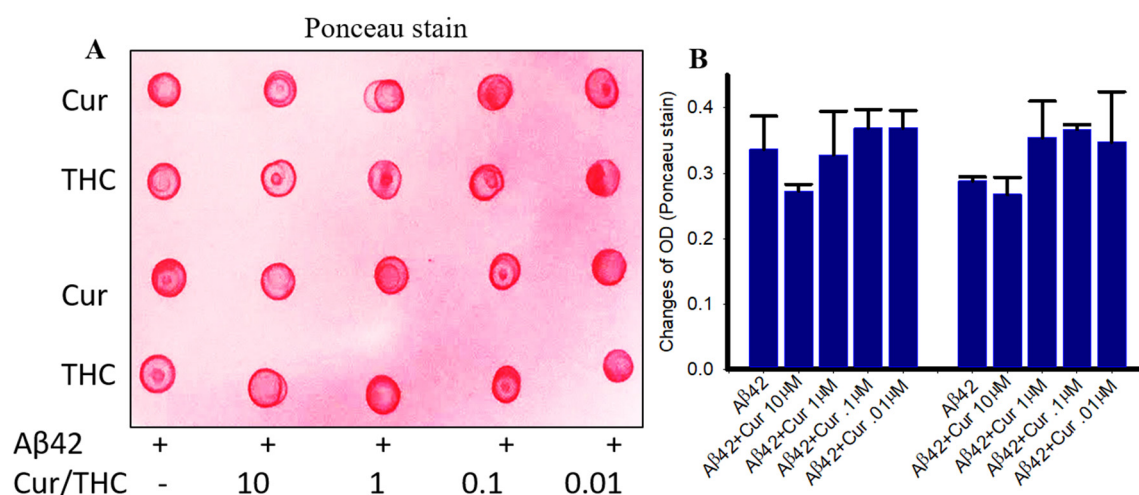


Figure S2. Ponceau stained dot blot. After loading 10 μ L of A β 42 peptide solution from each group on the nitrocellulose membrane, the blot was stained with Ponceau stain. **A:** Representative image of dot blot after Ponceau stain. **B:** No significant changes in optical density among the groups were observed.

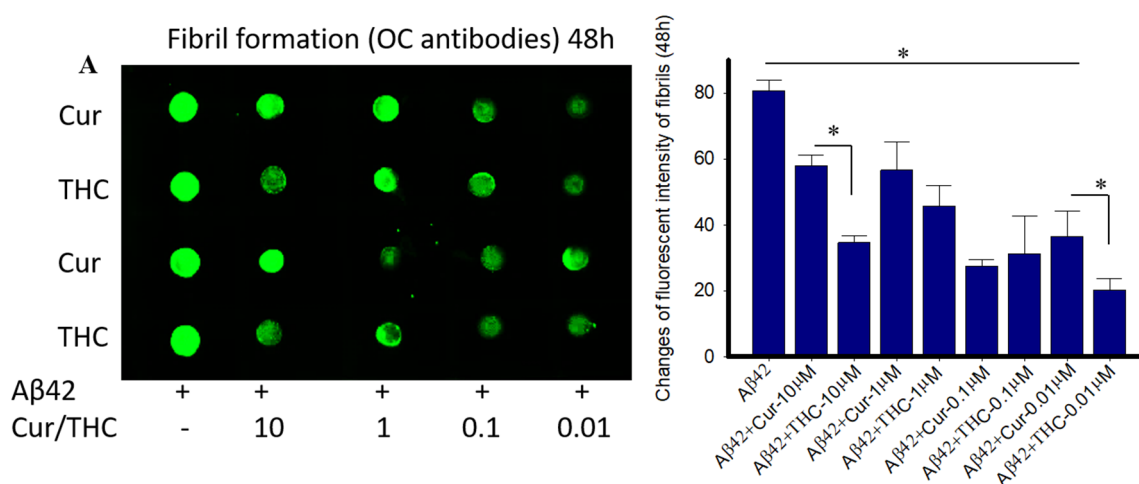


Figure S3. THC inhibited A β 42 fibrils formation greater than Cur. A β 42 peptide (40 μ M) was disaggregated with HFIP and dissolved in 60 mM of NaOH and diluted with PBS (pH7.4) and incubated for 24–48 h in presence or absence of different Cur-derivatives (1 μ M). Ten microliters of peptide from each group were spotted on nitrocellulose membrane, incubated with OC antibodies and probed with anti-rabbit antibodies conjugated with fluorophore 488 and the fluorescent intensity was recorded using a gel documentation system. **A:** Representative dot blot images after A β 42 was treated for 48 h with different concentrations of Cur and THC (in μ M: 10, 1, 0.1 and 0.001). **B:** THC showed greater inhibition for A β 42 fibril formation than Cur. * p <0.05 in comparison to untreated group and # p <0.05 in comparison to Cur-treated groups.