Supplementary Materials

The Homoleptic Curcumin–Copper Single Crystal (ML_2): A Long Awaited Breakthrough in the Field of Curcumin Metal Complexes

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1. Single crystal X-ray diffraction

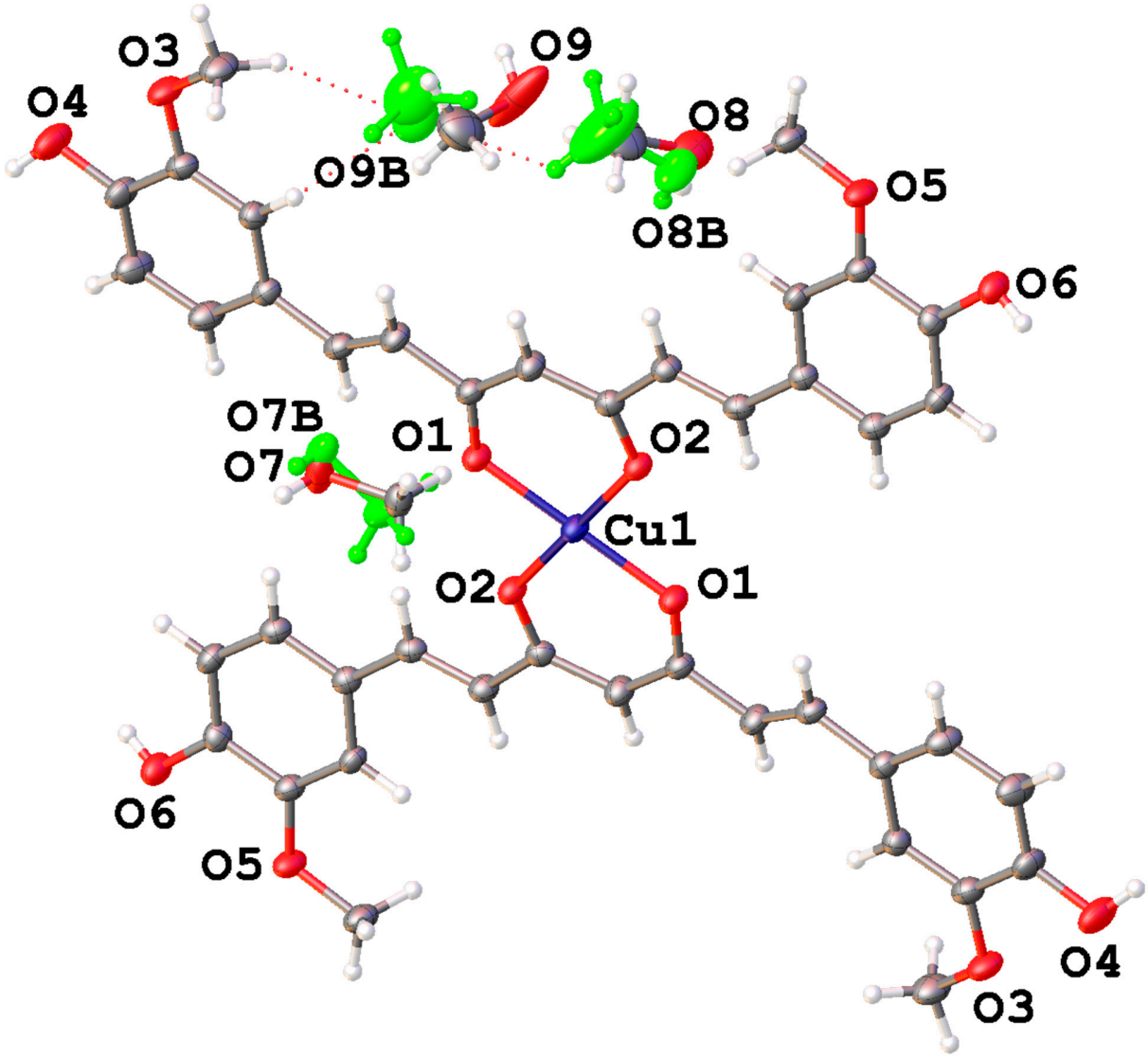


Figure S1. The molecular structure of complex **1** including molecules of solvent (methanol) and the disordered position of methanol (green ellipsoids).

Table S1. Crystallographic data of complex **1**.

Empirical Formula	**$C_{42}H_{38}O_{12}Cu\cdot 5MeOH$**
Formula weight	958.47
Temperature/K	130(2)
Crystal system	*triclinic*
Space group	P-1
a/Å	8.3372(7)
b/Å	8.7677(4)
c/Å	16.3052(12)
α/°	75.664(5)
β/°	84.240(6)
γ/°	84.636(5)
Volume/Å^3	1146.02(14)
Z	1
s_{calc} g/cm^3	1.389
μ/mm^{-1}	0.551
F(000)	505.0
Crystal size/mm^3	0.33 × 0.13 × 0.06
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	6.852 to 59.284
Index ranges	-11 ≤ h ≤ 11, -12 ≤ k ≤ 11, -22 ≤ l ≤ 22
Reflections collected	25565
Independent reflections	5848 [R_{int} = 0.0466, R_{sigma} = 0.0476]
Data/restraints/parameters	5848/120/377
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0498, wR_2 = 0.1160
Final R indexes [all data]	R_1 = 0.0706, wR_2 = 0.1293

2. Electrospray ionization

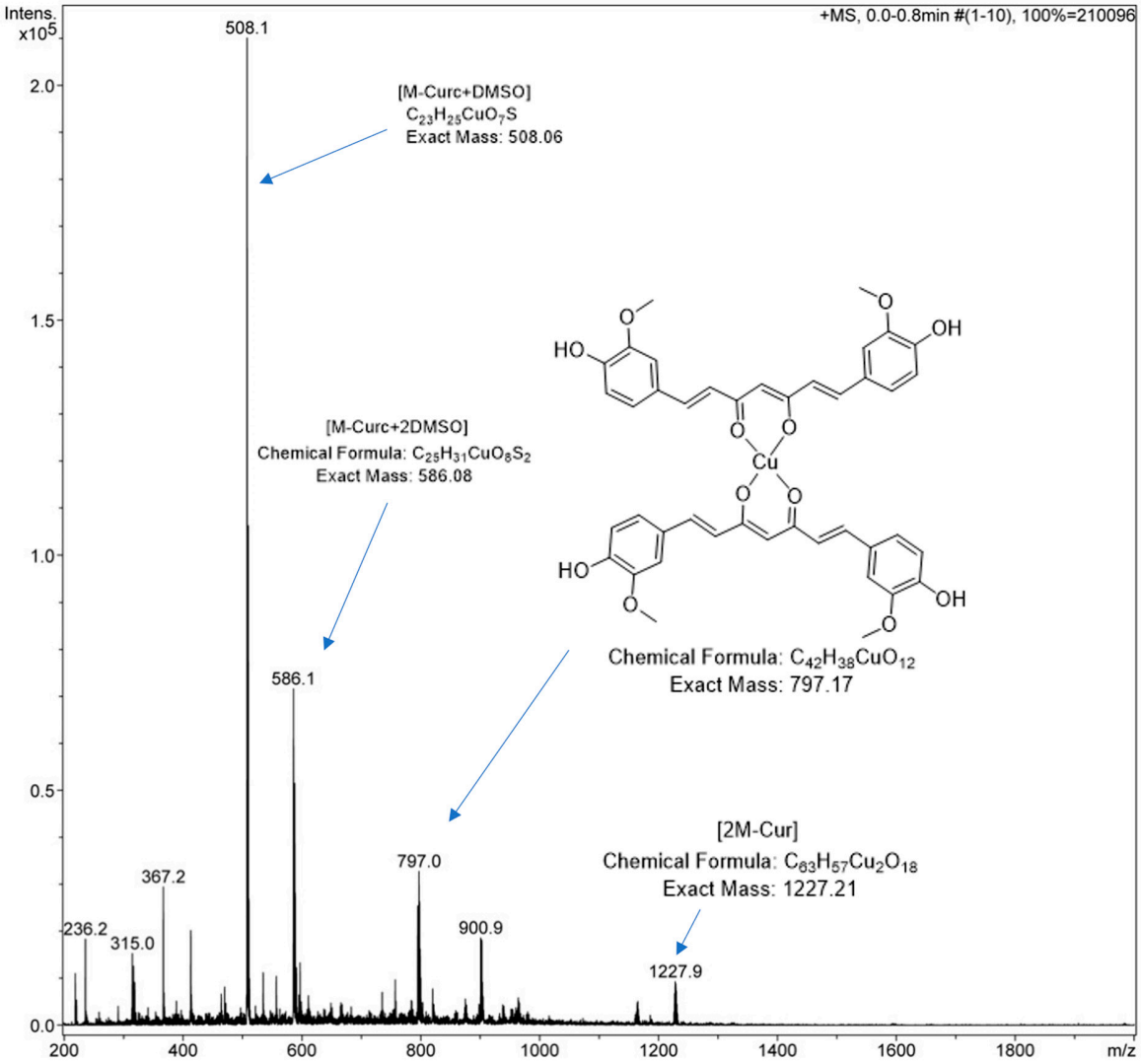


Figure S2. Mass spectrum of complex **1** (dark brown solid) by ESI^+ previously dissolved in DMSO.

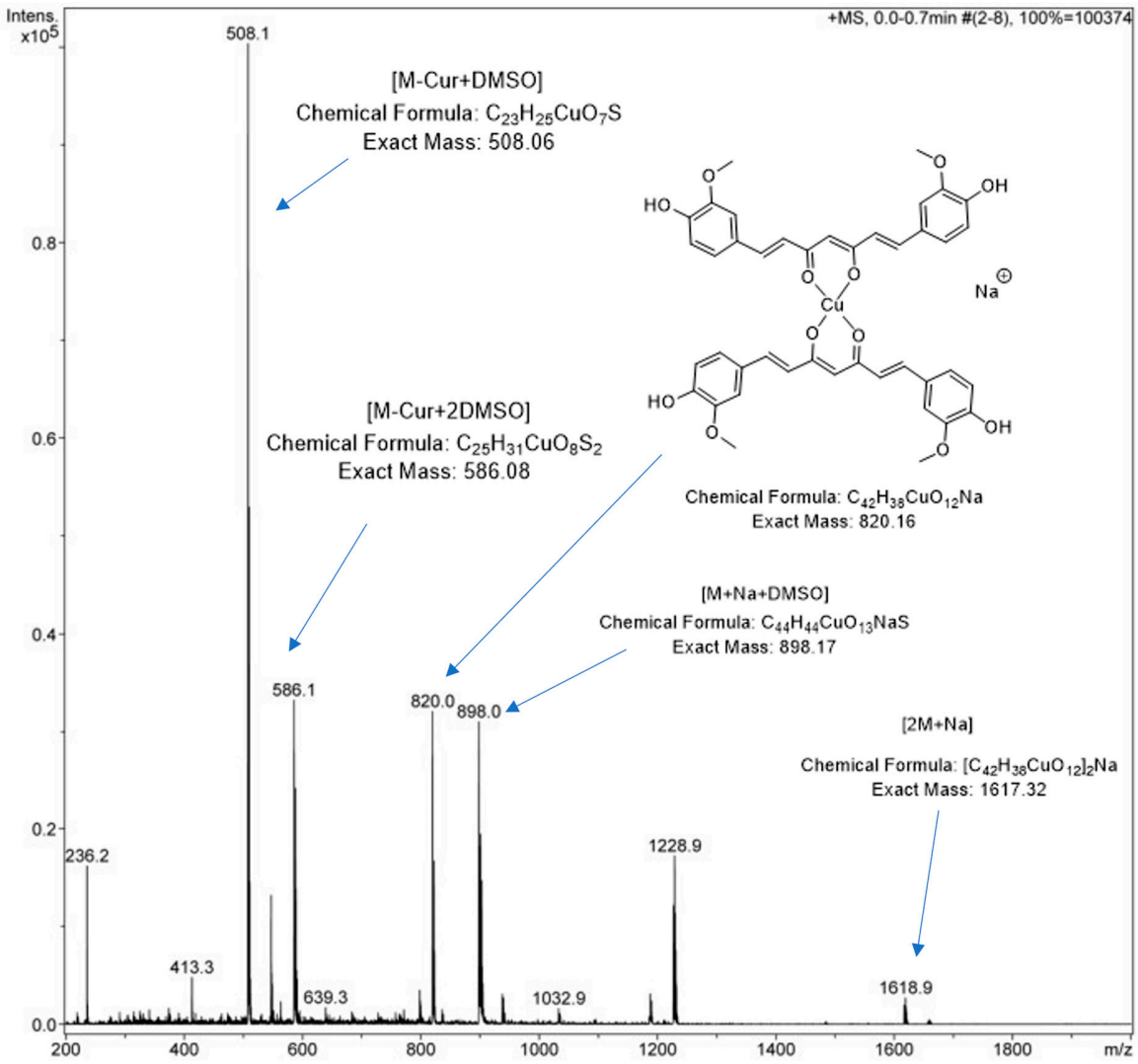


Figure S3. Mass spectrum of complex **1** (brilliant brown solid) by ESI$^+$ previously dissolved in DMSO.

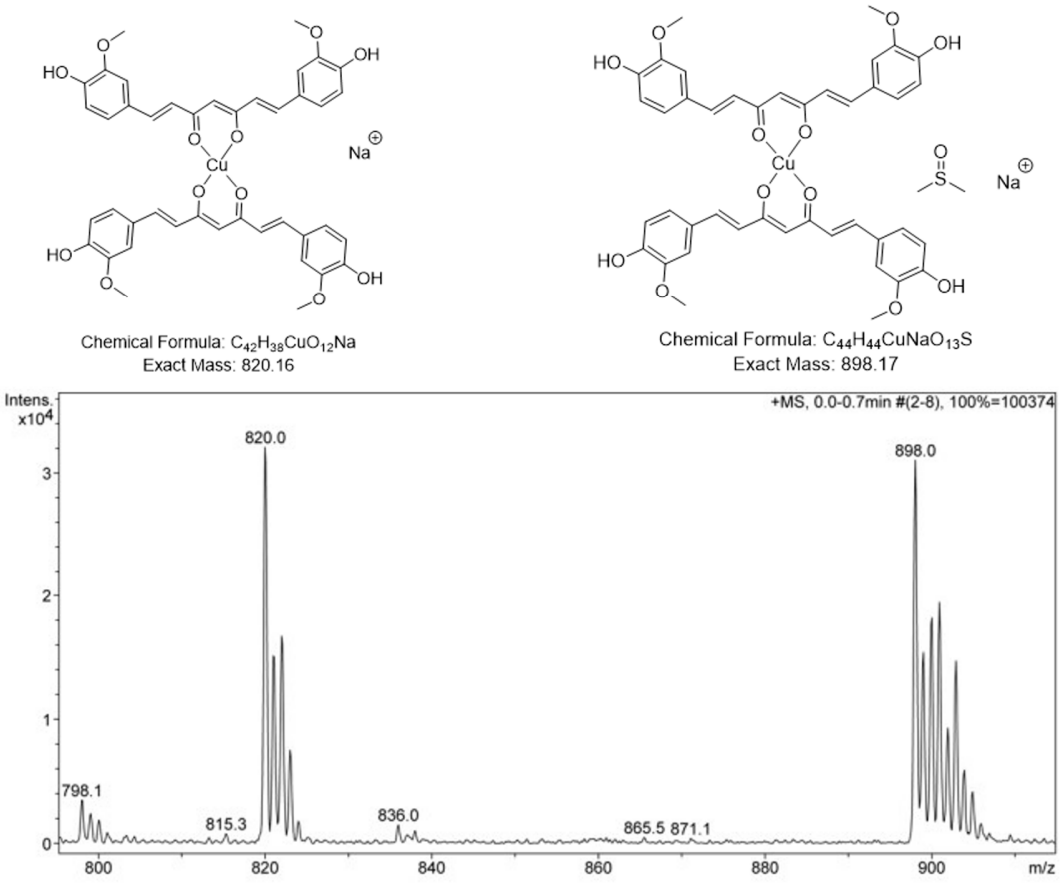


Figure S4. Amplification of Mass spectrum of complex **1** (brilliant brown solid) by ESI^+ previously dissolved in DMSO.

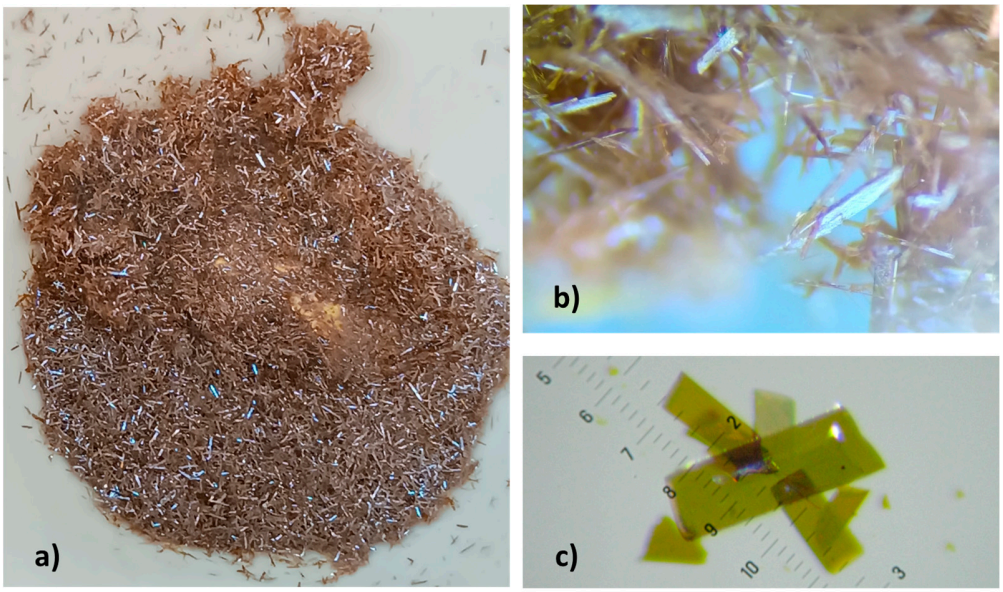


Figure S5. Grow process of a monocrystal of complex **1**: (**a**) Recrystallization of the filtrate and filtration in a Hirsch funnel, (**b**) amplified view of crystals, and (**c**) Monocrystals obtained after slow evaporation in methanol.

3. EPR and CP/MAS

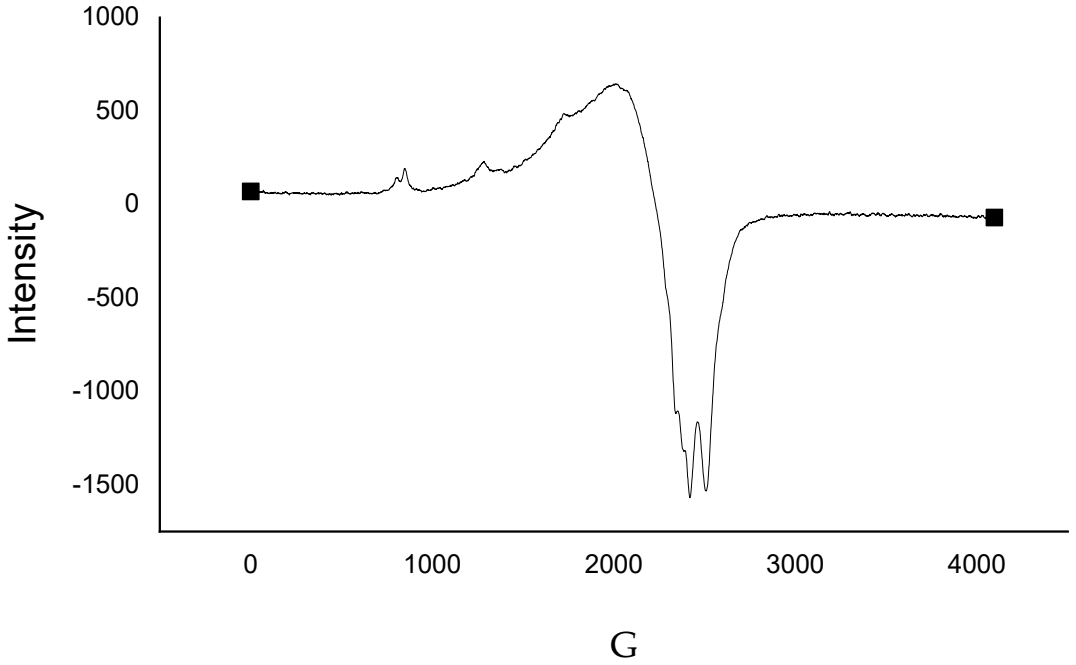


Figure S6. Solid state Electron Paramagnetic Resonance of amorphous material (dark brown solid).

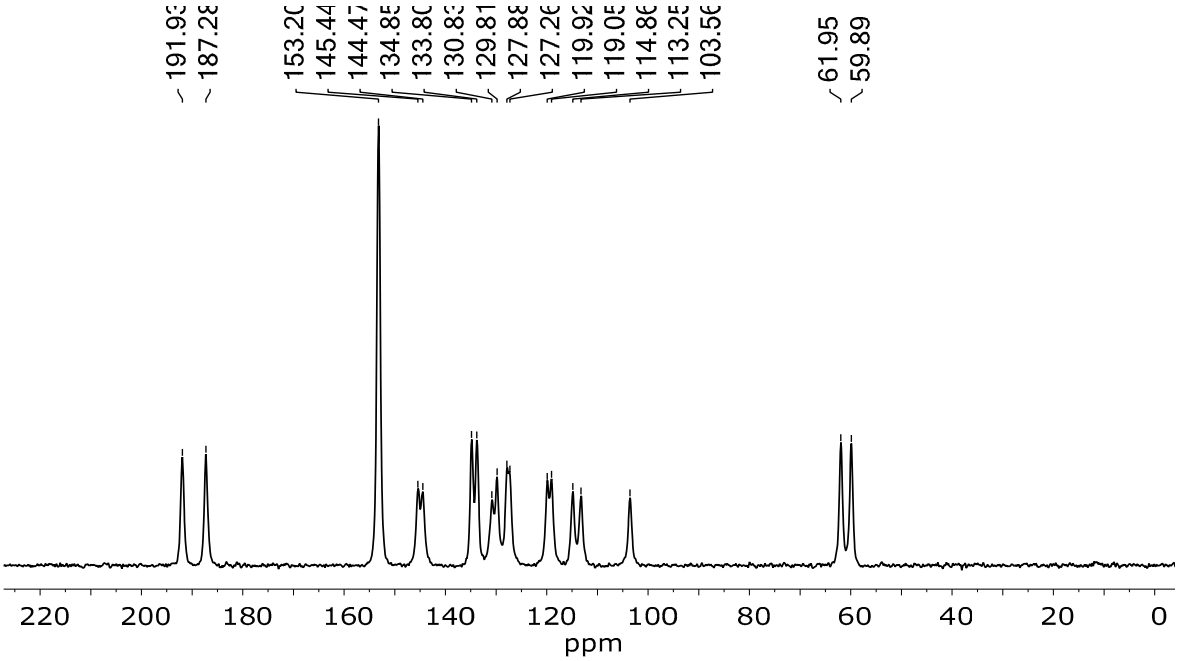


Figure S7. ^{13}C CP/MAS spectrum of curcumin.

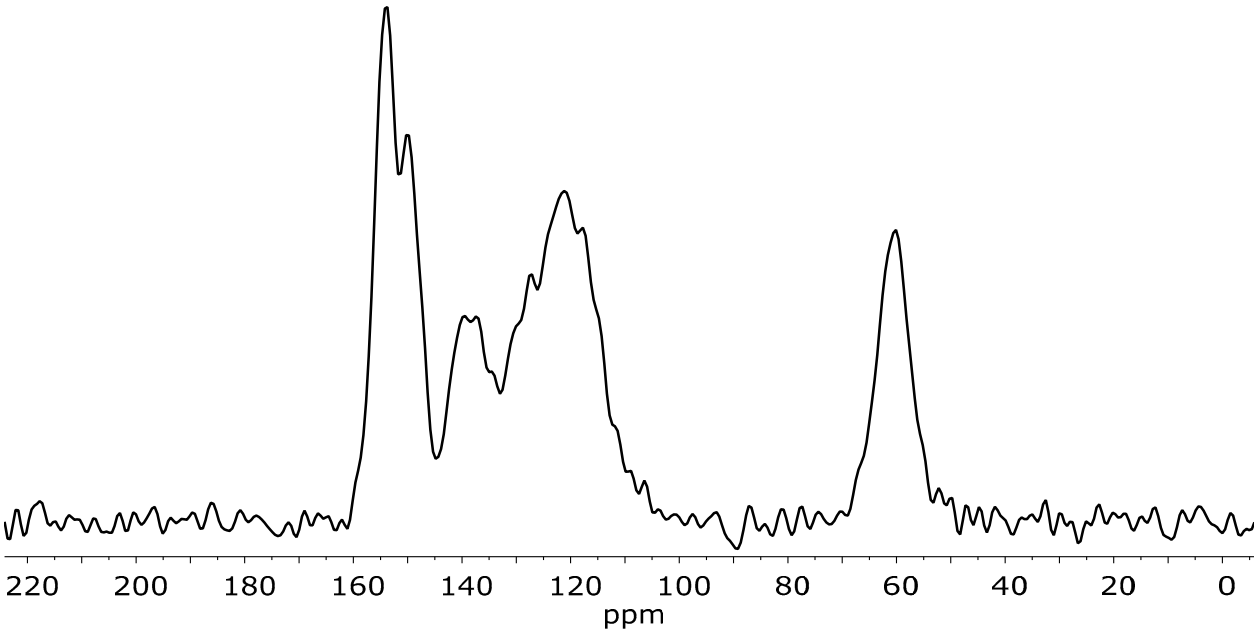


Figure S8. ^{13}C CP/MASS spectrum of complex (**1**).

4. IR (ATR)

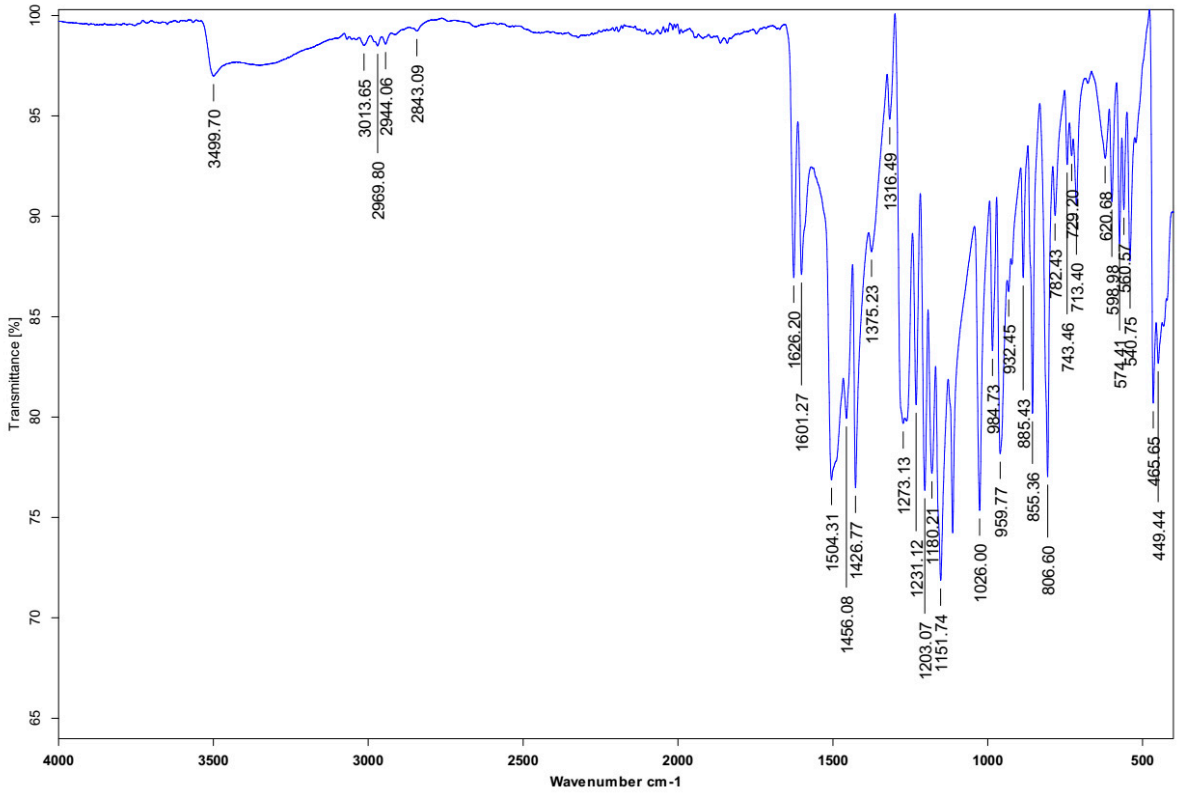


Figure S9. IR-ATR spectrum of free curcumin.

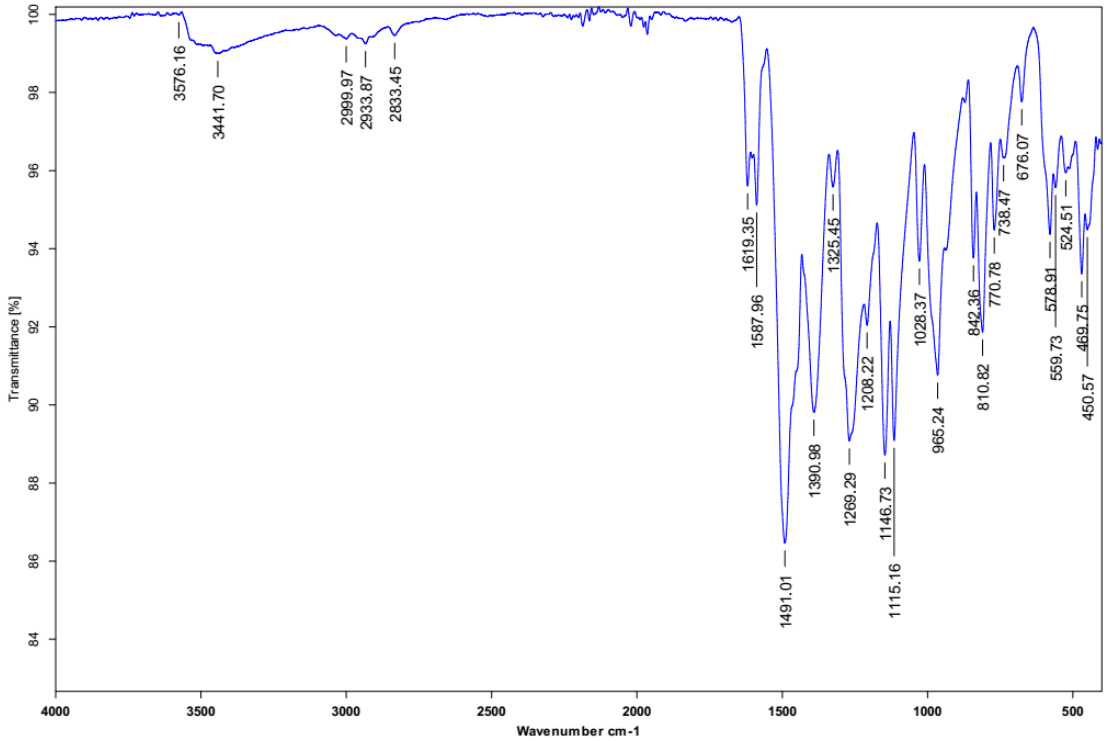


Figure S10. IR-ATR spectrum of complex (**1**) dark brown solid.

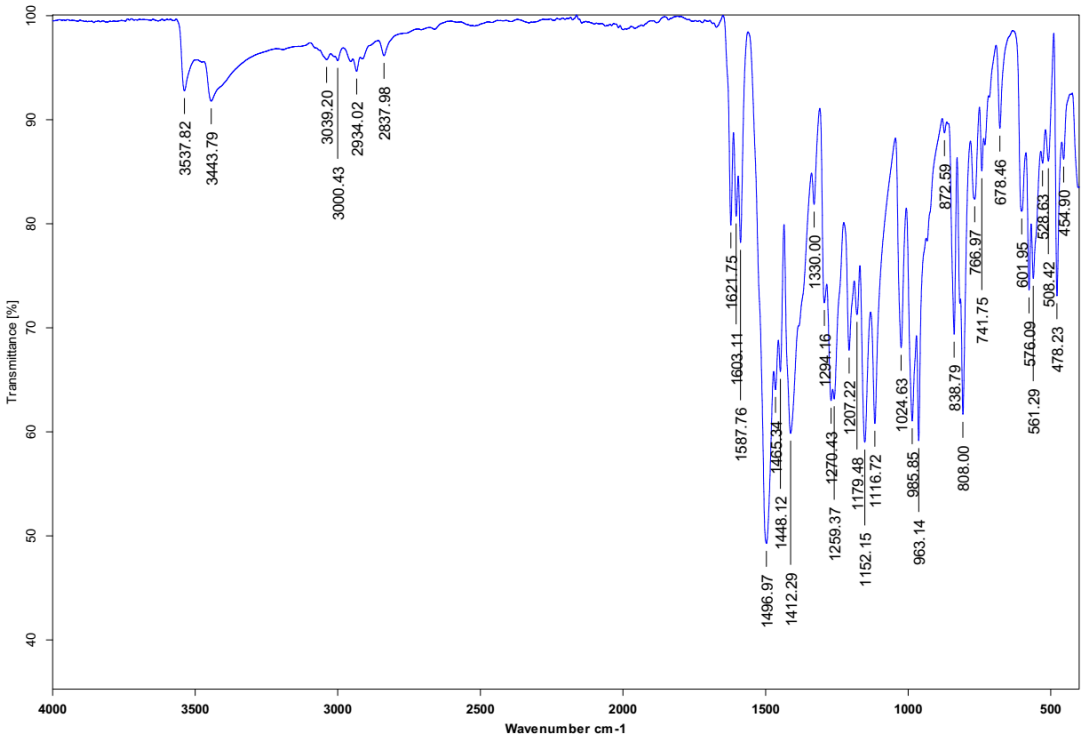


Figure S11. IR-ATR spectrum of complex (**1**) brilliant brown crystalline solid.

5. UV-Vis

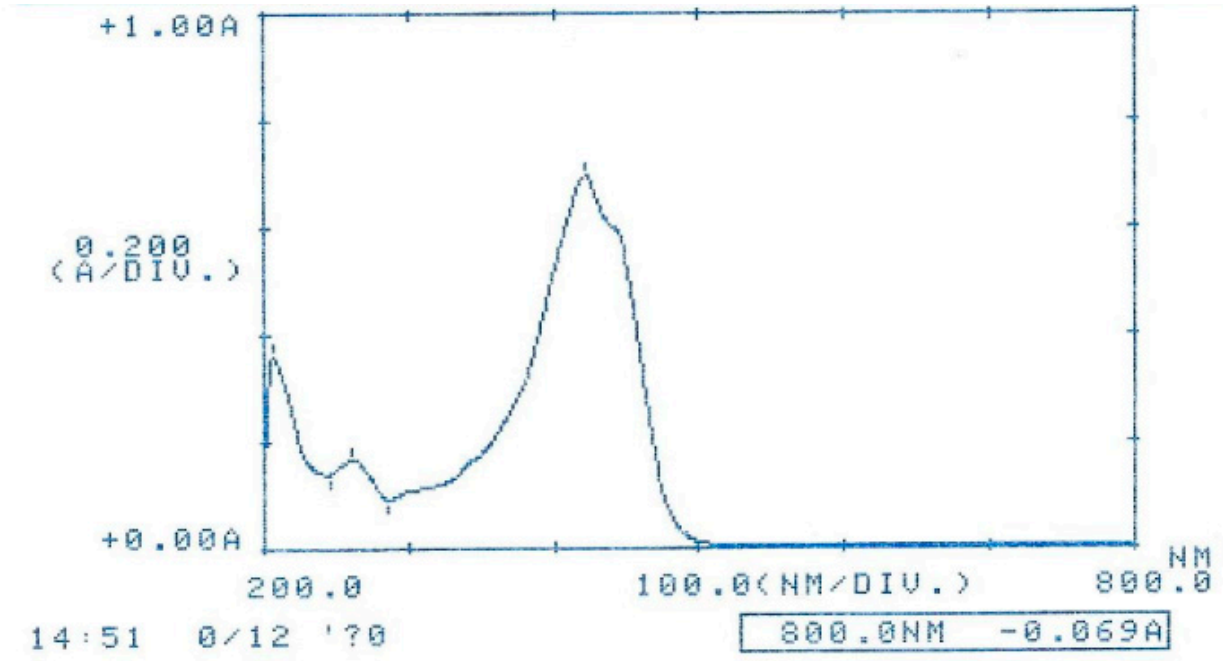


Figure S12. UV-Vis spectrum of complex (**1**) dark brown solid (REF: Methanol, Max= 422 nm).

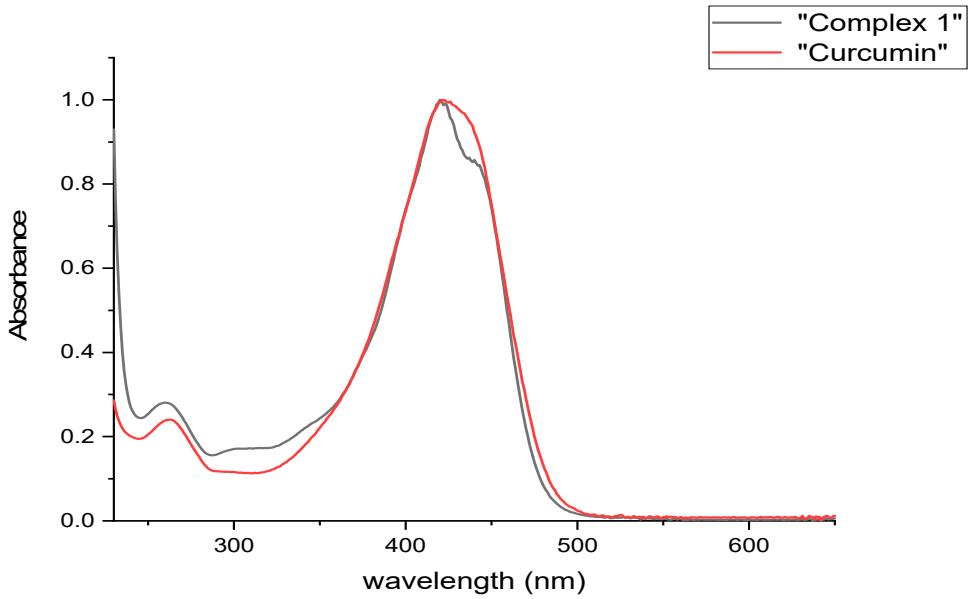


Figure S13. UV-Vis spectra of complex (**1**) brilliant brown crystalline solid (REF: Methanol, Max= 421 nm) and free curcumin (REF: Methanol, Max= 420 nm).

6. PXRD

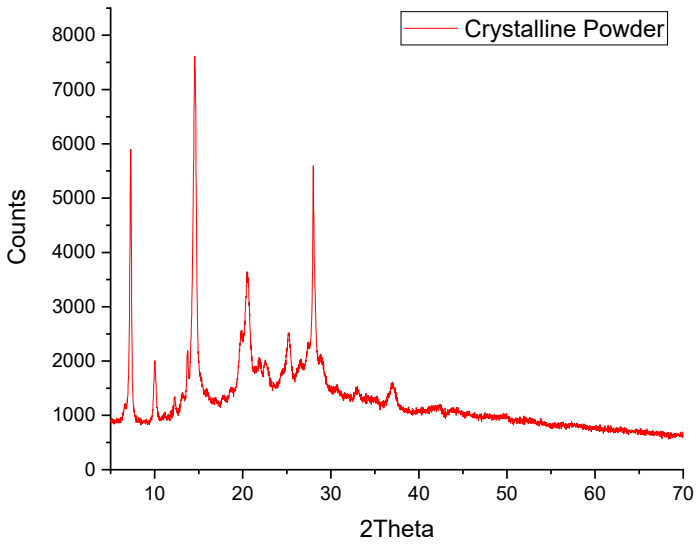


Figure S14. Powder XRD pattern of complex **1** (bright brown material).

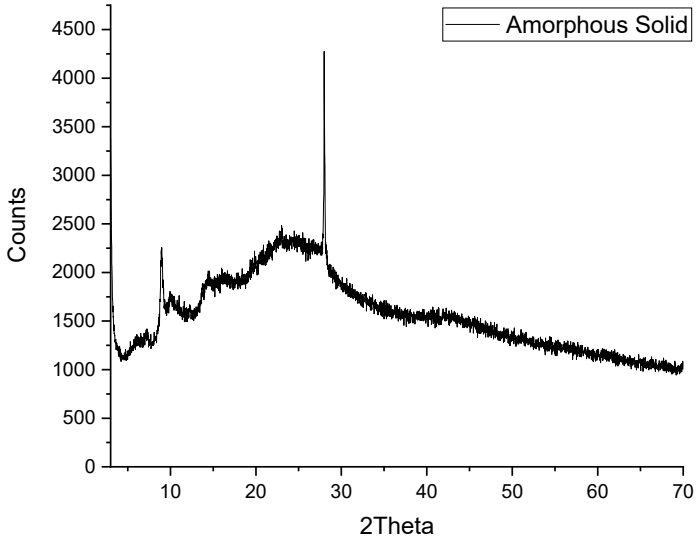


Figure S15. Powder XRD pattern of complex **1** (amorphous solid).

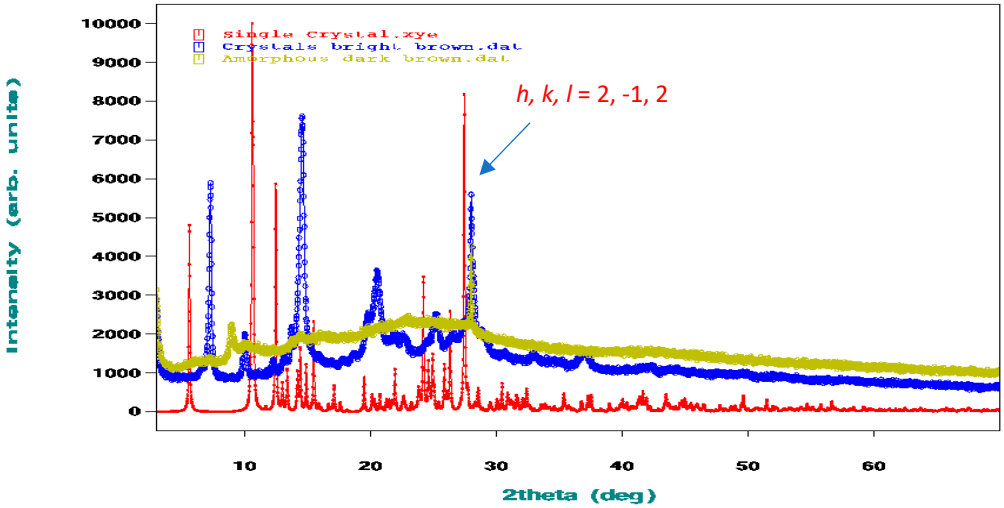
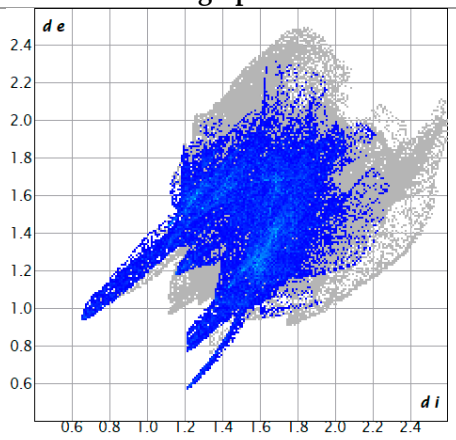
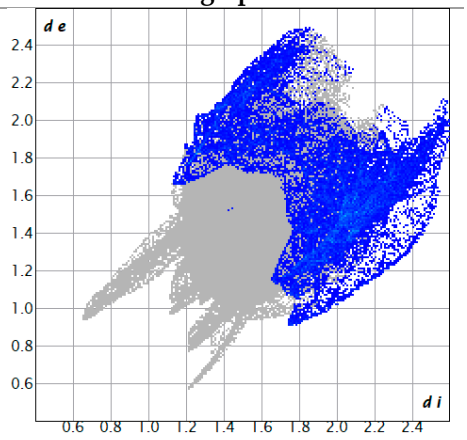
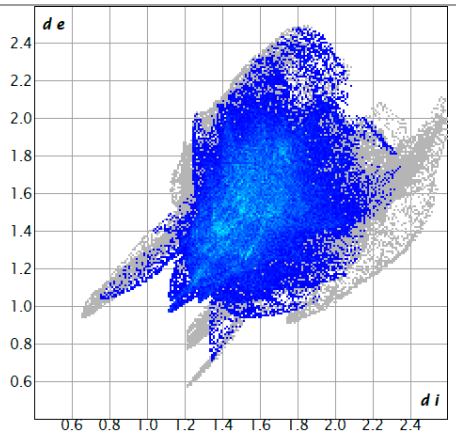
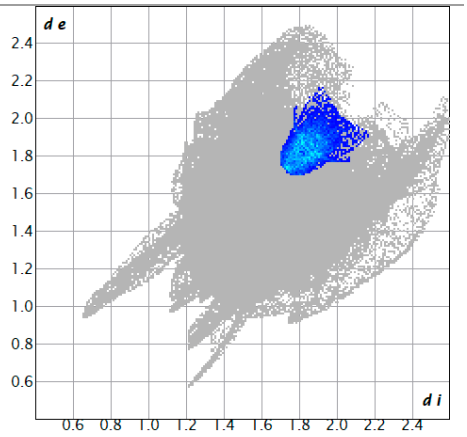


Figure S16. Comparison of PXRD patterns of complex **1** (red: simulated, 130K); blue: crystalline material; gold: amorphous material).

7. Fingerprints plots

Contact	Fingerprint	Contact	Fingerprint
O···H/H···O 24.5%		C···H/H···C 17.8 %	
H···H 44.2 %		C···C 7.4 %	

8. Cytotoxicity

Table S2. Growth inhibition percentages of cancerous and noncancerous (COS-7) cell lines by compounds (9.9 μM, 48 h).

	Grow inhibition (%) by cell line						
Sample	**U251**	**PC-3**	**K562**	**HCT-15**	**MCF-7**	**SKLU-1**	**COS 7**
Curcumin	NC	22.7	20.81	10.5	1.30	5.8	5.05
Complex 1	35.43	29.3	62.87	18.8	0.55	26.1	20.35

Inhibition percentages of complex **1** relative to curcumin. Growth inhibition percentages of cancerous and noncancerous (COS-7) cell lines by compounds. U251 (human glioblastoma), PC-3 (human prostatic adenocarcinoma), K562 (human chronic myelogenous leukaemia), HCT-15 (human colorectal adenocarcinoma), MCF-7 (human mammary adenocarcinoma), cell lines were supplied by the National Cancer Institute (USA); and SKLU-1 (human lung adenocarcinoma) and COS-7 cell line (monkey African green kidney) were donated by the Cancer Institute of Mexico. *The results are the average of three runs.

9. Antioxidant activity

Table S3. Inhibition of Lipid Peroxidation on Rat Brain.

Sample	**Concentration (mM)**	**TBARS (nmol/mg prot.)**	**Inhibition (%)**	**IC_{50} (mM)**
Complex 1	Basal	0.319±0.051		
	Control	9.038±0.512		
	0.18	7.759±0.548	14.27±2.02	1.24±0.08
	0.32	7.242±0.492*	19.98±1.14*	
	0.55	6.230±0.488**	31.24±1.80**	
	0.99	4.987±0.315**	44.81±1.88**	
	1.76	3.239±0.342**	63.61±5.30**	
	3.12	1.766±0.525**	79.69±6.78**	
	5.55	0.622±0.053**	93.02±0.91**	

	9.87	0.353±0.072**	96.16±0.58**	
Curcumin	Basal	0.319±0.051		
	Control	9.038±0.512		
	0.18	8.345±0.412	7.58±1.12	3.03±0.15
	0.32	8.136±0.403	9.88±1.97	
	0.56	7.542±0.462	16.6±0.39	
	1	6.932±0.418**	23.32±1.34**	
	1.78	6.100±0.322**	32.48±0.39**	
	3.16	4.267±0.093**	52.46±3.01**	
	5.62	2.289±0.343**	74.11±5.04**	
	10	0.881±0.286**	89.84±3.81**	
BHT	Basal	0.268±0.053		
(n=3)	Control	7.384±0.630		
	0.56	6.098±0.353	16.64±2.86	1.22±0.44
	0.75	5.559±0.294*	23.92±2.69*	
	1	4.457±0.283**	37.14±7.44**	
	1.33	3.228±0.572**	53.59±8.93**	
	1.78	1.315±0.489**	81.59±6.89**	
	2.37	0.487±0.075**	93.16±1.16**	

Homogenised in: PBS; Vehicle: DMSO; Experiment: Curve; Peroxidation: induced with $FeSO_4$ 10 mM, Incubation time: 1 h; EDTA: 2 mM. The values represent the average of three independent experiments ± standard error of the media $(\bar{x} \pm ES)$. Data were subjected to an analysis of variance (ANOVA) followed by a Dunnett pass to isolate groups with significant differences. The values of $p \leq 0.05$ (*) and $p \leq 0.01$ (**) were considered as significant differences with respect to control.

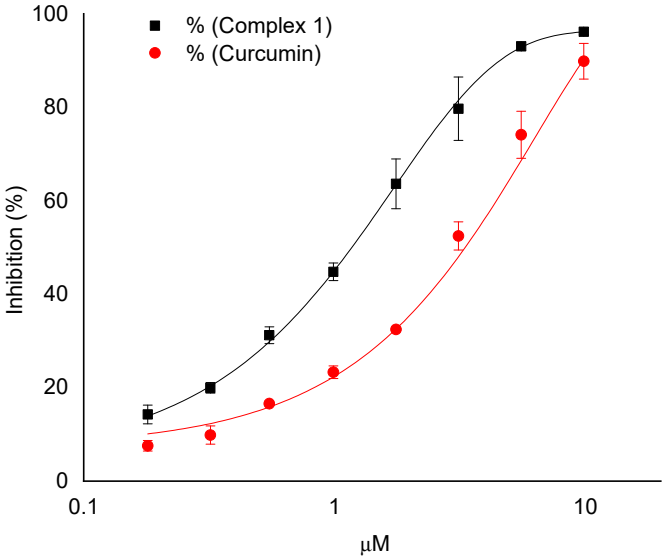


Figure S17. Inhibition curve of Lipid Peroxidation on Rat Brain.

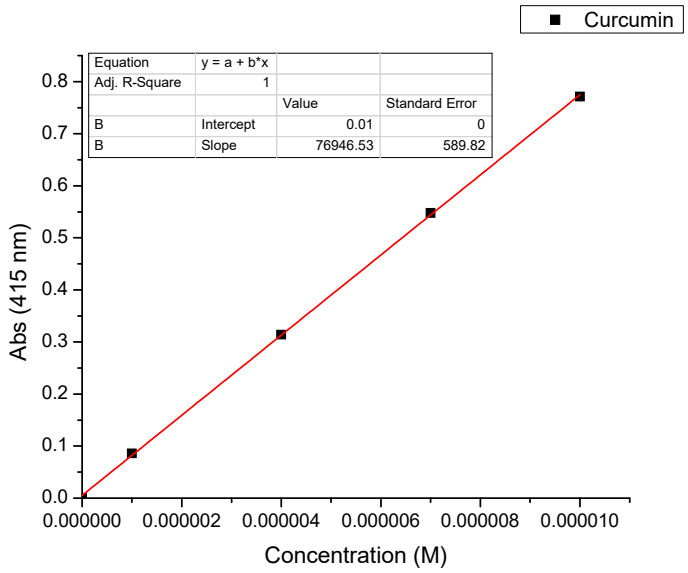


Figure S18. Adj. R-Square of Curcumin in 1-Octanol.

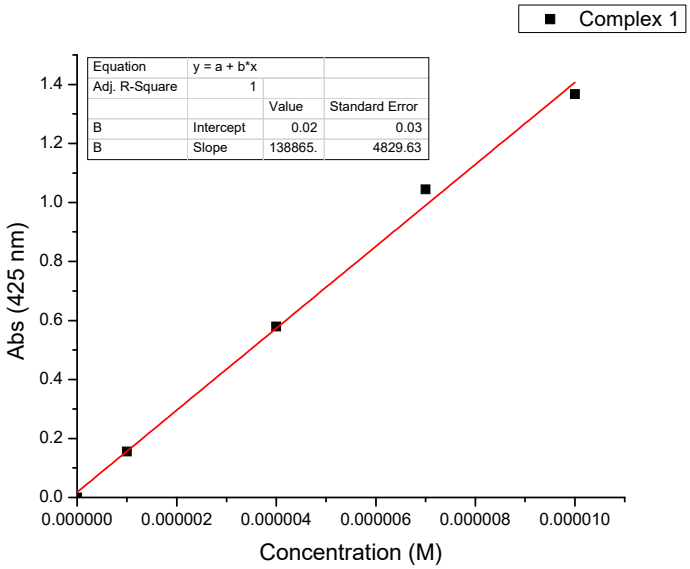


Figure S19. Adj. R-Square of **Complex 1** in 1-Octanol.