Electronic Supplementary information (ESI): Biodegradable Self-assembly Micelles Significantly Enhanced Solubility, Biological Stability and *in vivo* Antitumor Efficacy of Hexylselen

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Table S1. The Solubility of CPD-3B in Different Solvents (25 ℃, n ≥ 3)

Dissolving substances		Solubility (mg/mL)
Aqueous solvent	Water	0.0016 ± 0.00005
	HCl solution (pH=1.2)	0.0022 ± 0.00026
	Sodium Acetate buffer (pH=4.5)	0.0013 ± 0.00047
	Phosphate Buffer Saline (pH=7.4)	0.0008 ± 0.00015
Hydrophilic solvent	DMSO	33.81 ± 0.70
	DMF	17.31 ± 0.32
	MeOH	1.41 ± 0.13
	EtOH	1.28 ± 0.04
	Acetonitrile	0.42 ± 0.005
	Acetone	0.44 ± 0.04
	Isopropyl Alcohol	0.98 ± 0.06
Hydrophobic solvent	Ethyl Acetate	0.24 ± 0.02
	1-Octanol	1.06 ± 0.08
	DCM	3.17 ± 0.16
Liquid excipient	Propylene glycol	1.05 ± 0.02
	Glycerine	0.04 ± 0.001
	PEG200	2.95 ± 0.07
	PEG400	2.38 ± 0.08
	Tween20	1.06 ± 0.02
	Tween80	0.51 ± 0.02
Solid excipients (10% solution)	Poloxamer 188 (F68)	0.013 ± 0.003
	Poloxamer 407 (F127)	0.098 ± 0.008
	Soluplus	0.515 ± 0.008
	Hyropropyl-β-Cyclodextrin (HP-β-CD)	0.060 ± 0.003
	Sulfobutylether-β-Cyclodextrin (SBE -β-CD)	0.071 ± 0.004
	PEG2000	0.007 ± 0.002
	PEG4000	0.008 ± 0.001
	PEG6000	0.006 ± 0.001

Table S2. The Inhibition Tumor Cell Growth by CPD-3B@SOL Micelles

Samples	H22 (IC_{50}: μM)	A549 (IC_{50}: μM)
Free CPD-3B	1.51 ± 0.04	1.39 ± 0.07
CPD-3B@SOL micelles	1.75 ± 0.02	2.79 ± 0.18
Blank SOL micelles	＞ 30	＞ 30

Table S3. The $t_{1/2}$ and Clearance rates of CPD-3B vehicle and CPD-3B@SOL micelles in liver microsomes (n ≥ 3)

Samples	Fitted equation	k_e	$t_{1/2}$ (h)	CL (L/h/g)
Free CPD-3B	lnC = -1.1204t + 4.4351; R^2 = 0.9782	-1.1204	0.62	134.4
CPD-3B@SOL micelles	lnC = -0.1298t + 4.4975; R^2 = 0.9505	-0.1298	5.34	15.6
Coumarin	lnC = -0.5783t + 4.6404; R^2 = 0.9922	-0.5783	1.20	69.4

Notes: k_e: the slope of the relationship of lnC (compound concentration) and t (incubated time); $t_{1/2}$: half-time life; CL_{int}: intrinsic Clearance.

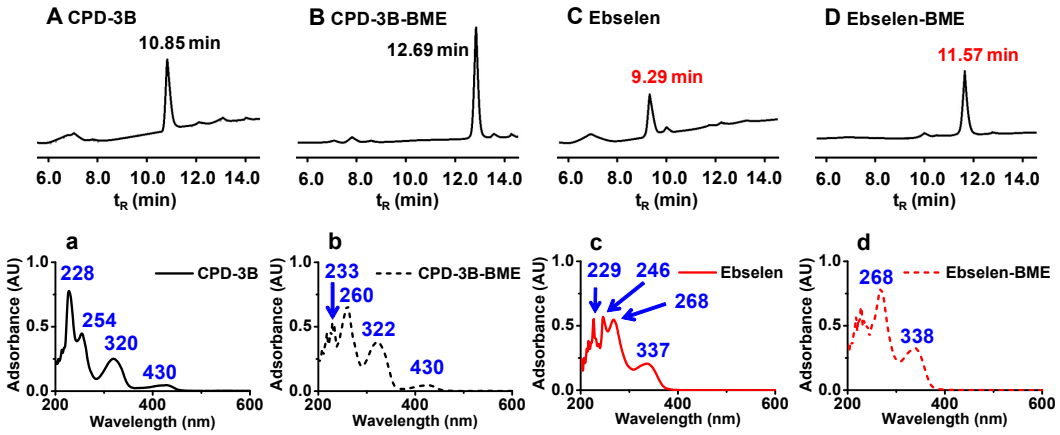

Figure S1. The HPLC (A, B, C, D) and UV (a, b, c, d) Spectrograms of CPD-3B, Ebselen, CPD-3B BME Derivative and Ebselen BME Derivative.

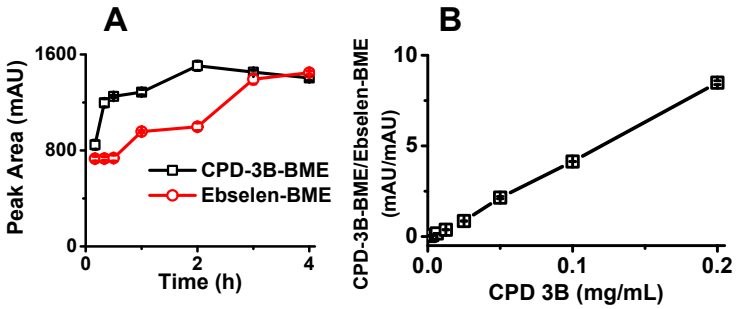

Figure S2. The Correlation of Peak Area to deriving time (A-t) of CPD-3B-BME and Ebselen-BME and Standard Curve for CPD-3B Quantification. A: The optimizing derivatization time for CPD-3B and Ebselen; B: The standard curve for quantifying CPD-3B by CPD-3B-BME and internal standard Ebselen-BME: Peak areas of CPD-3B-BME (A_m) and Ebselen-BME (A_n), and the relation of A_m/A_n to C_{CPD-3B} produced equation A_m/A_n= 42.984C - 0.1155, R^2=0.9995, range of 1-200 μg/mL.