

Figure S1. (A) Viability of HCCLM3 cells treated with the 20 compounds (<30% cell viability). (B) The viability of Huh7 cells treated with these 20 compounds. (C and D) Wound healing assay. The HCCLM3 and Huh7 cells were pre-treated with PPVI or Static. PPVI, polyphyllin VI; STAT3, signal transducer and activator of transcription 3.

A		HCCLM3	B		Huh7
Name		Cell viability	Name		Cell viability
Corypalmine		0.60%	Bardoxolone methyl		1.50%
cis-Aconitic acid		0.72%	Polyphyllin VII		3.19%
Loureirin A		0.72%	Polyphyllin VI		7.25%
Polyphyllin VI		3.54%	β -Lapachone		8.78%
β -Lapachone		4.29%	Tomatine		9.88%
Tomatine		5.15%	Solamargine		17.52%
Polyphyllin II		7.14%	Gambogic Acid		18.23%
Tubeimoside II		8.32%	Betulin		25.31%
Solamargine		9.21%	Lapachol		53.60%
Bardoxolone Methyl		10.69%	Catharanthine		54.08%
Polyphyllin VII		12.86%	Nerolidol		56.72%
Gambogic Acid		19.62%	Tectoridin		61.36%
Aristolochic acid A		21.45%	Tubeimoside II		71.92%
Catharanthine		22.31%	Polyphyllin II		73.56%
Betulin		23.92%	Aristolochic acid A		90.46%
Nerolidol		24.22%	Corypalmine		94.21%
Tectoridin		24.36%	Ononin		98.28%
Ononin		27.93%	Angoroside C		100.78%
Lapachol		30.86%	cis-Aconitic acid		103.81%
Angoroside C		31.41%	Loureirin A		106.07%

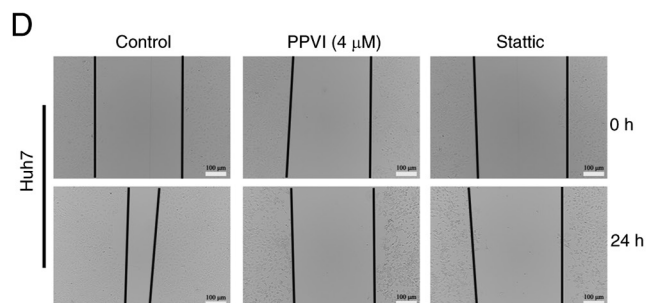
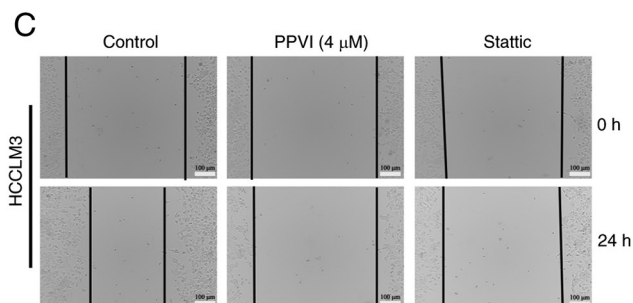


Figure S2. PPVI inhibits the STAT3/GPX4 axis in hepatocellular carcinoma cells. The HCCLM3 and Huh7 cells were pre-treated with PPVI or Stattic. (A) ROS levels in HCCLM3 and Huh7 cells were observed using DHE. (B) The Fe²⁺ content in HCCLM3 and Huh7 cells was detected using a FerroOrange fluorescent probe. (C and D) MDA and GSH levels. (E and F) Protein expression of GPX4 in HCCLM3 and Huh7 cells was detected using immunofluorescence staining. *P<0.05, **P<0.01, ***P<0.001 and ****P<0.0001 vs. control or as indicated. NS, not significant; Con, control; PPVI, polyphyllin VI; STAT3, signal transducer and activator of transcription 3; GPX4, glutathione peroxidase 4; DHE, dihydroethidium; ROS, reactive oxygen species; GSH, glutathione; MDA, malondialdehyde.

