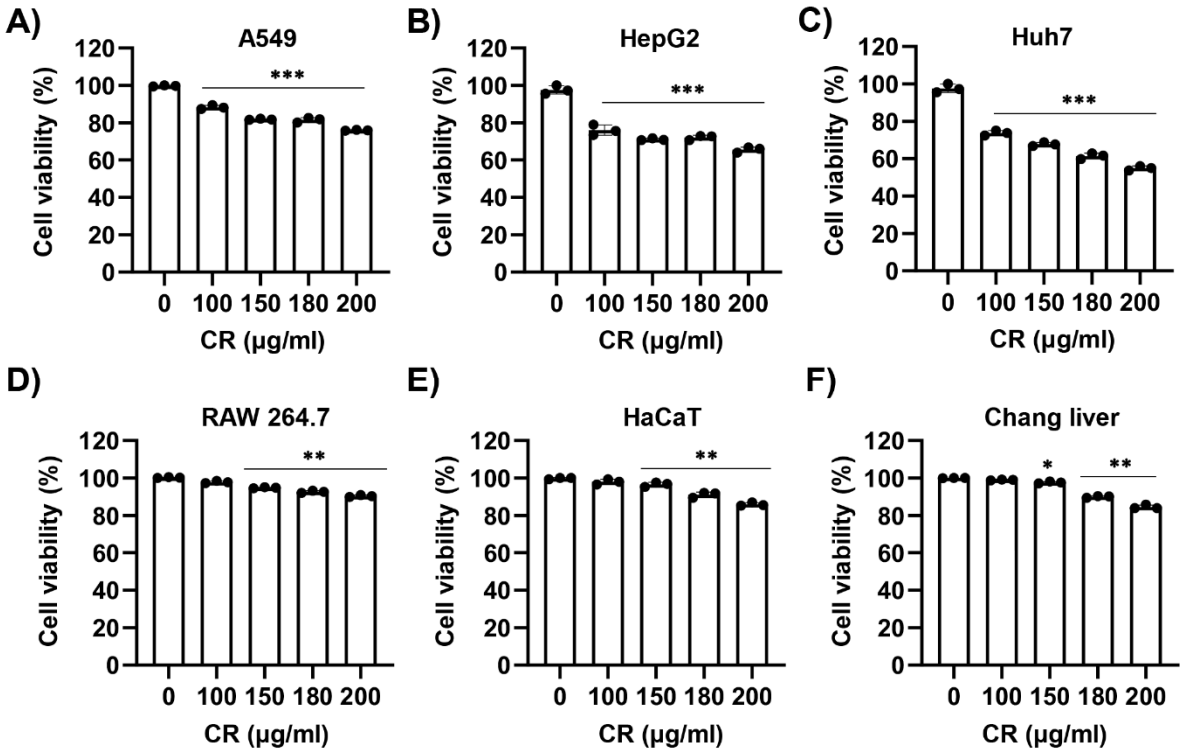
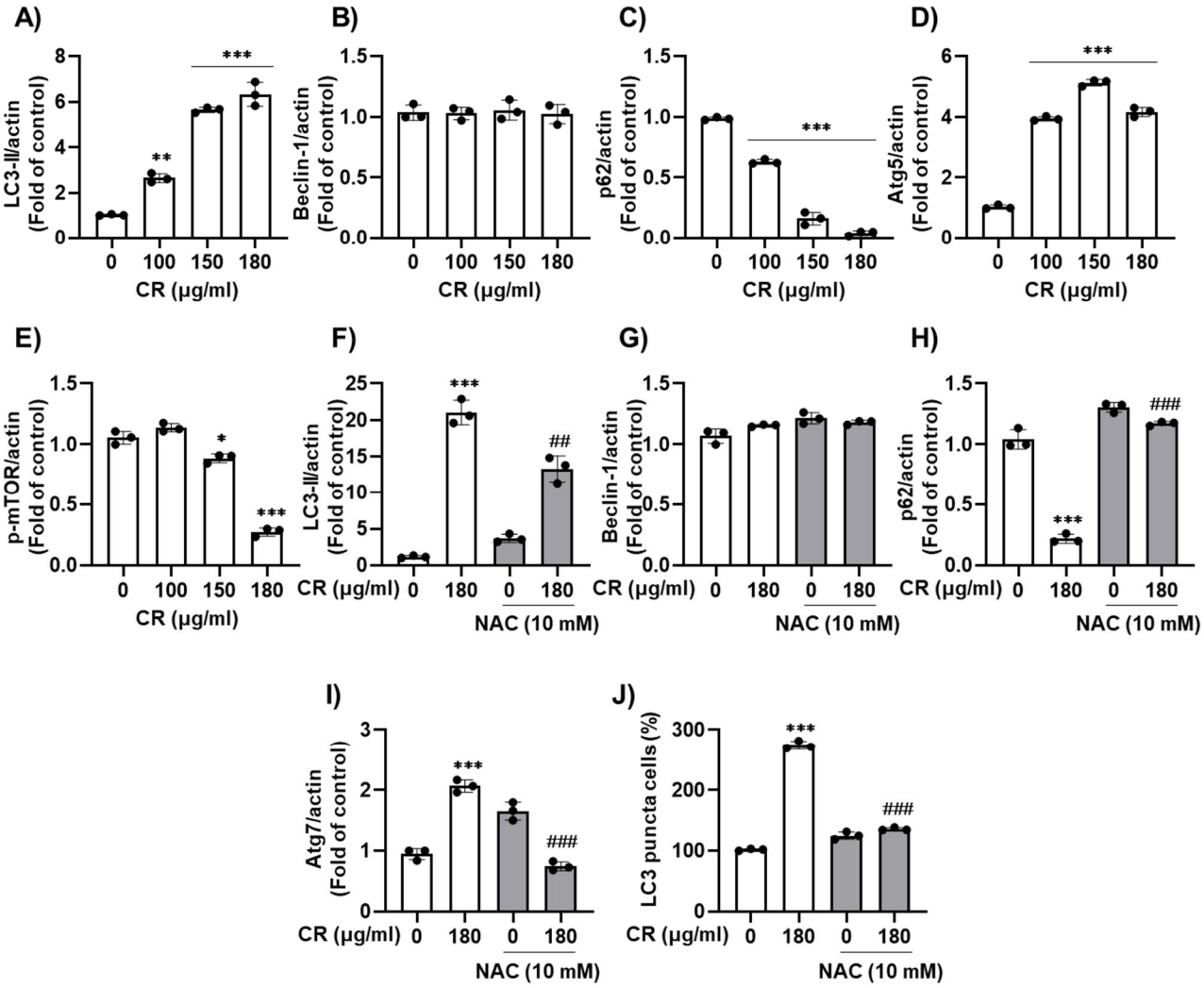


Supplementary Figure S1. Effect of Coptidis Rhizoma ethanol extract (CR) on cell viability in the various cell lines. Various concentrations of CR were treated on human lung cancer A549 cells (**A**), human hepatoma HepG2 cells (**B**), human hepatoma Huh7 cells (**C**), mouse macrophage RAW 264.7 cells (**D**), human keratinocyte HaCaT cells (**E**) and normal Chang liver cells (**F**). After 24 h, the cell viability was assessed by an MTT assay. Each bar represents the mean ± SD of three independent experiments (n = 3). * $p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$ compared to untreated cells.



Supplementary Figure S2. Effect of Coptidis Rhizoma ethanol extract (CR) on autophagy. (**A**–**E**) Hep3B cells were treated with indicated concentration of CR for 24 h. (**F**–**I**) Hep3B cells were pre-treated with or without N-acetylcysteine (NAC), ROS inhibitor, for 1 h, and then treated with 180 μg/mL of CR for 24 h. Bar graphs indicate the relative band density in western blot analysis (n = 3). (**J**) Hep3B cells were pre-treated with or without N-acetylcysteine (NAC), ROS inhibitor, for 1 h, and then treated with 180 μg/mL of CR for 24 h. Bar graphs indicate the relative LC3 puncta in immunofluorescence (n = 3). * $p < 0.05$ and *** $p < 0.001$ compared to untreated cells; # $p < 0.05$, ## $p < 0.01$ and ### $p < 0.001$ compared to CR-treated cells.

Supplementary Table S1. The effect of oral administration of CR on organ weights in Hep3B xenograft model.

Group	Organ weights (g)				
	Heart	**Lung**	**Liver**	**Kidney**	**Spleen**
Normal	0.110 ± 0.08	0.138 ± 0.019	0.894 ± 0.111	0.258 ± 0.034	0.091 ± 0.017
Control	0.110 ± 0.015	0.139 ± 0.017	0.955 ± 0.115	0.256 ± 0.027	0.139 ± 0.042
CR 100	0.105 ± 0.008	0.132 ± 0.011	0.933 ± 0.064	0.266 ± 0.015	0.113 ± 0.026
CR 200	0.106 ± 0.011	0.140 ± 0.017	0.979 ± 0.127	0.280 ± 0.027	0.125 ± 0.043
Sorafenib	0.111 ± 0.008	0.132 ± 0.007	0.964 ± 0.152	0.296 ± 0.023	0.101 ± 0.027

After 14 days of orally administered with treatments, each organ (heart, lung, liver, kidney and spleen) was isolated from CR (n = 10) or sorafenib (n = 6), and non-treated (n = 10) xenograft mice as well as normal (n = 5) mice and measured the weight. Data are presented as means ± SD. All data showed no statistically significant difference between all groups.

Supplementary Table S2. Changes in the hematological and biochemical profiles in Hep3B xenograft model.

Parameter (units)	Group				
	Normal	**Control**	**CR 100**	**CR 200**	**Sorafenib**
RBC (× 10^3 cells/μL)	8.13 ± 0.35	8.28 ± 0.33	8.18 ± 0.43	8.60 ± 0.48	8.23 ± 0.33
WBC (× 10^3 cells/μL)	1.58 ± 0.73	1.70 ± 0.77	1.3 ± 0.78	1.64 ± 0.73	0.72 ± 0.67
Hemoglobin (g/dL)	11.58 ± 6.12	13.92 ± 0.86	13.72 ± 1.04	14.55 ± 0.79	14.48 ± 0.53
Hematocrit (%)	43.28 ± 1.85	43.63 ± 1.98	42.08 ± 2.37	44.82 ± 1.60	43.98 ± 1.90
MCV (fL)	53.20 ± 0.70	52.68 ± 1.75	51.47 ± 0.98	52.18 ± 1.99	53.48 ± 0.47
MCH (pg)	14.18 ± 7.40	16.80 ± 0.70	16.77 ± 0.69	16.95 ± 0.66	17.58 ± 0.38
MCHC (g/dL)	26.63 ± 13.91	31.88 ± 0.61	32.55 ± 0.90	32.50 ± 0.73	32.93 ± 0.92
RDW (%)	13.70 ± 0.59	13.33 ± 1.11	12.72 ± 0.31	12.88 ± 0.55	13.37 ± 0.30
MPV (fL)	10.75 ± 1.03	10.27 ± 0.40	9.95 ± 0.65	9.82 ± 0.34	9.98 ± 0.26
PLT (× 10^3 cells/μL)	804 ± 84	885 ± 73	924 ± 93	880 ± 234	827 ± 97
ALT (U/L)	101.00 ± 4.73	119.22 ± 23.20	109.28 ± 14.07	102.80 ± 13.84	126.78 ± 15.38
AST (U/L)	15.48 ± 1.10	18.97 ± 5.70	20.30 ± 4.41	20.07 ± 5.73	25.37 ± 3.00
ALP (U/L)	438.08 ± 88.15	311.37 ± 120.10	303.30 ± 66.62	335.93 ± 47.70	421.02 ± 152.86
BUN (mg/dL)	19.47 ± 2.01	18.21 ± 3.79	20.66 ± 3.12	22.96 ± 3.37	22.22 ± 2.67
Creatinine (mg/dL)	0.34 ± 0.02	0.32 ± 0.02	0.33 ± 0.03	0.32 ± 0.03	0.34 ± 0.03

After 14 days of orally administered with treatments, whole blood and serum of mice were collected from CR (n = 10), sorafenib (n = 6), non-treated (n = 10), and normal (n = 5) mice for hematological and biochemical assessment. Data are presented as means ± SD. All data showed no statistically significant difference between groups. RBC, red blood cells; WBC, white blood cells; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; NCHC, MCH concentration; RDW, red blood cell distribution width; MPV, mean platelet volume; PLT, platelet; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; BUN, blood urea nitrogen.