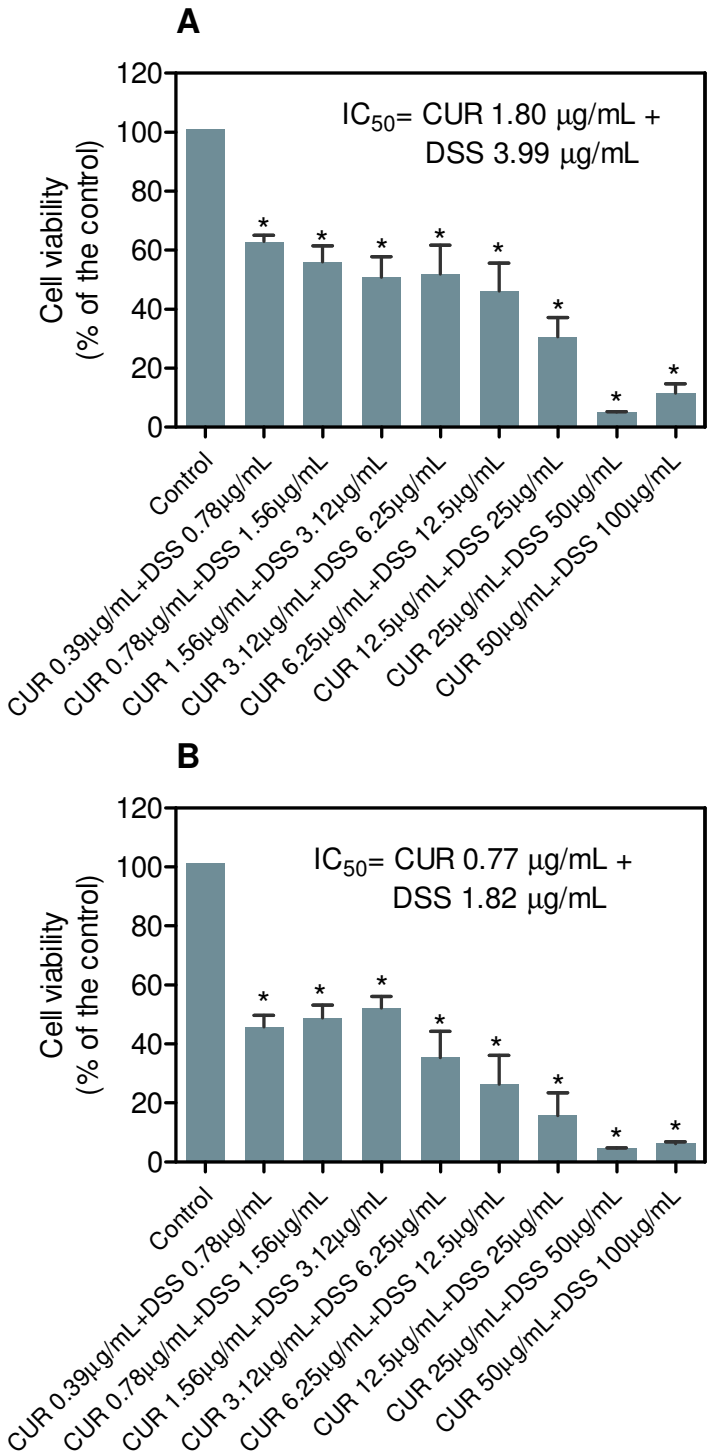

Figure S1. Effect of the combination of CUR and DSS at a ratio of 1:2 on the viability of B16-F10 (**A**) and MRC-5 (**B**) cells measured by the alamar blue method after 72 h of incubation. Data are shown as the mean ± S.E.M. of at least three independent experiments carried out in duplicate. *$P < 0.05$ compared with control (untreated cells) by ANOVA followed by Student Newman–Keuls test.

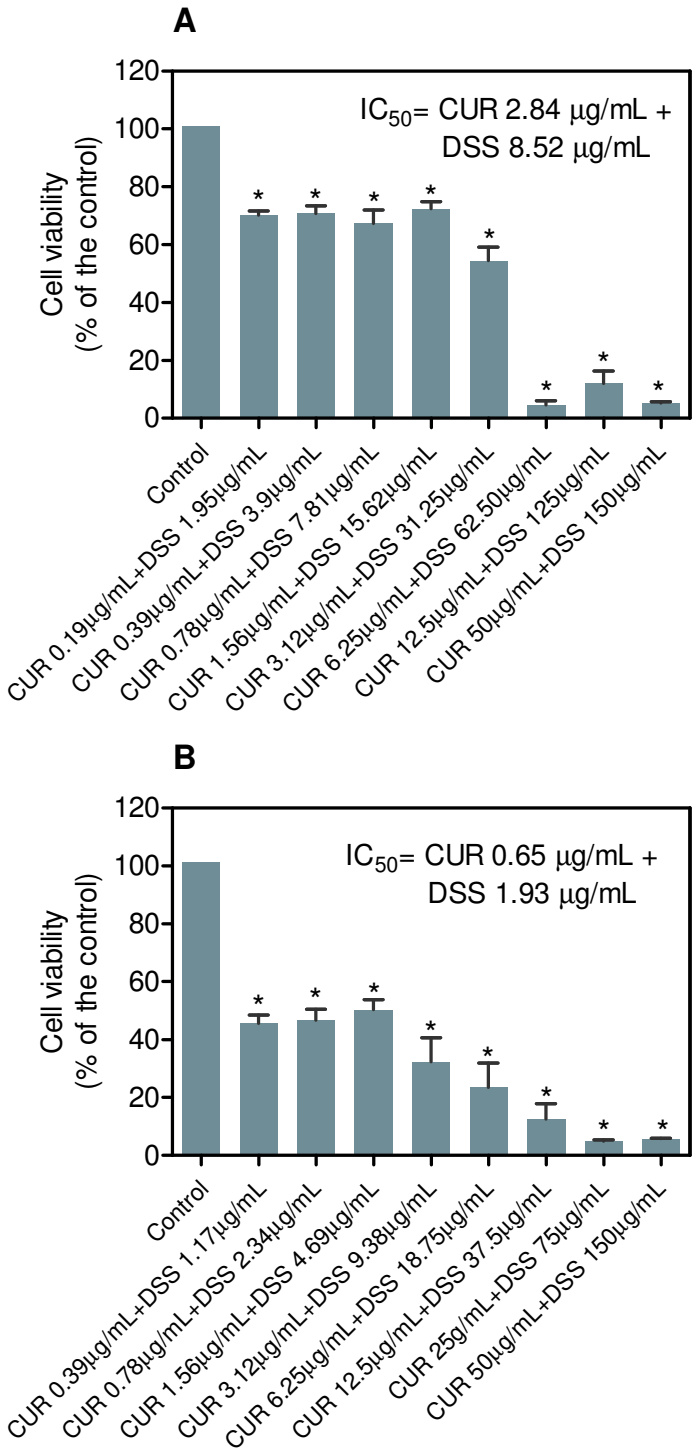

Figure S2. Effect of the combination of CUR and DSS at a ratio of 1:3 on the viability of B16-F10 (**A**) and MRC-5 (**B**) cells measured by the alamar blue method after 72 h of incubation. Data are shown as the mean ± S.E.M. of at least three independent experiments carried out in duplicate. *$P < 0.05$ compared with control (untreated cells) by ANOVA followed by Student Newman–Keuls test.

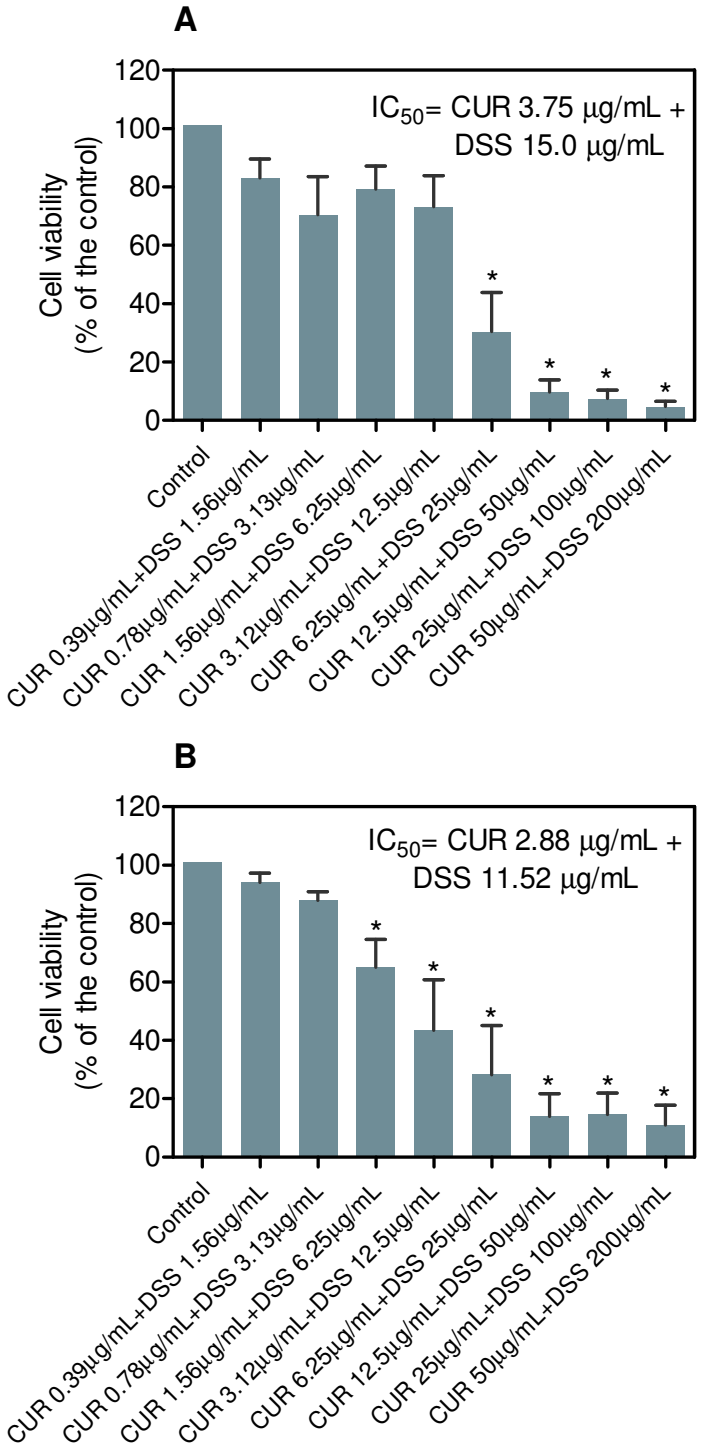

Figure S3. Effect of the combination of CUR and DSS at a ratio of 1:4 on the viability of B16-F10 (**A**) and MRC-5 (**B**) cells measured by the alamar blue method after 72 h of incubation. Data are shown as the mean ± S.E.M. of at least three independent experiments carried out in duplicate. *$P < 0.05$ compared with control (untreated cells) by ANOVA followed by Student Newman–Keuls test.

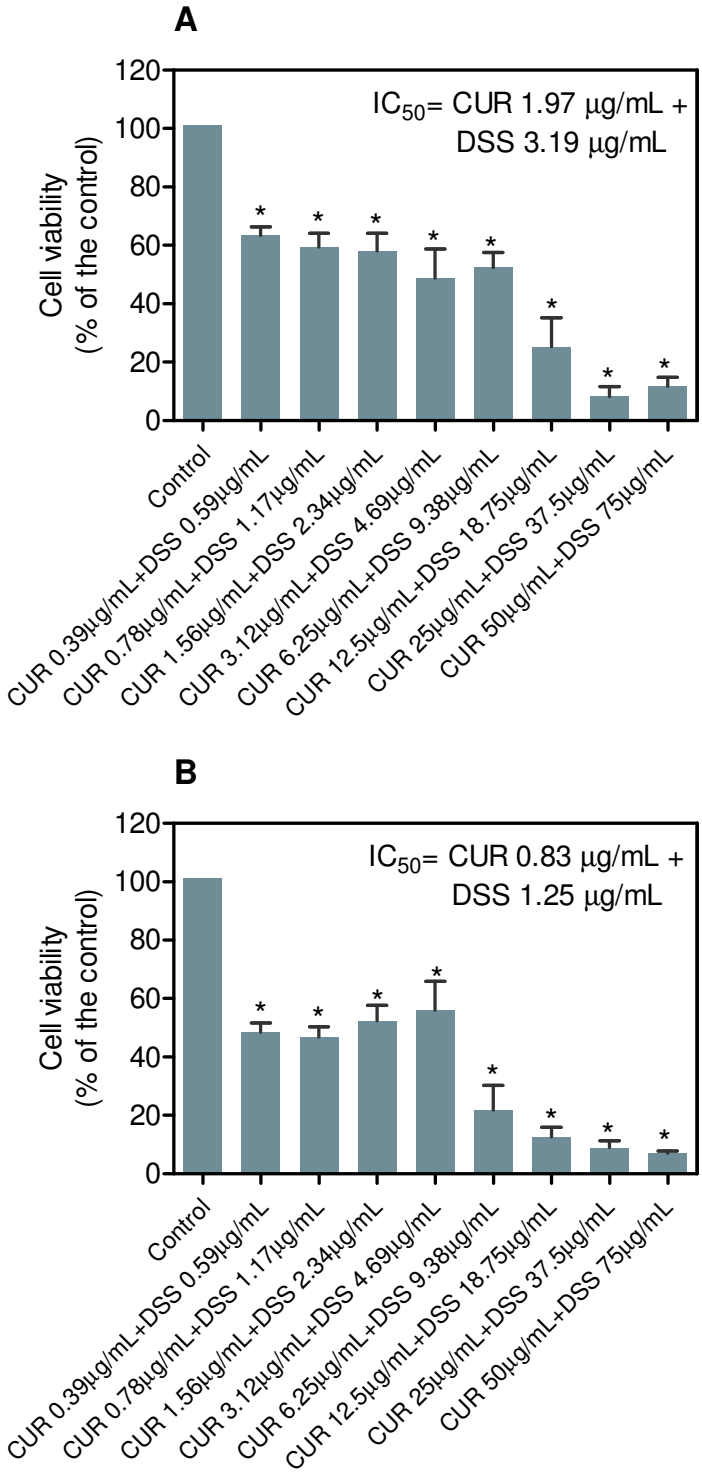

Figure S4. Effect of the combination of CUR and DSS at a ratio of 2:3 on the viability of B16-F10 (**A**) and MRC-5 (**B**) cells measured by the alamar blue method after 72 h of incubation. Data are shown as the mean ± S.E.M. of at least three independent experiments carried out in duplicate. *$P < 0.05$ compared with control (untreated cells) by ANOVA followed by Student Newman–Keuls test.

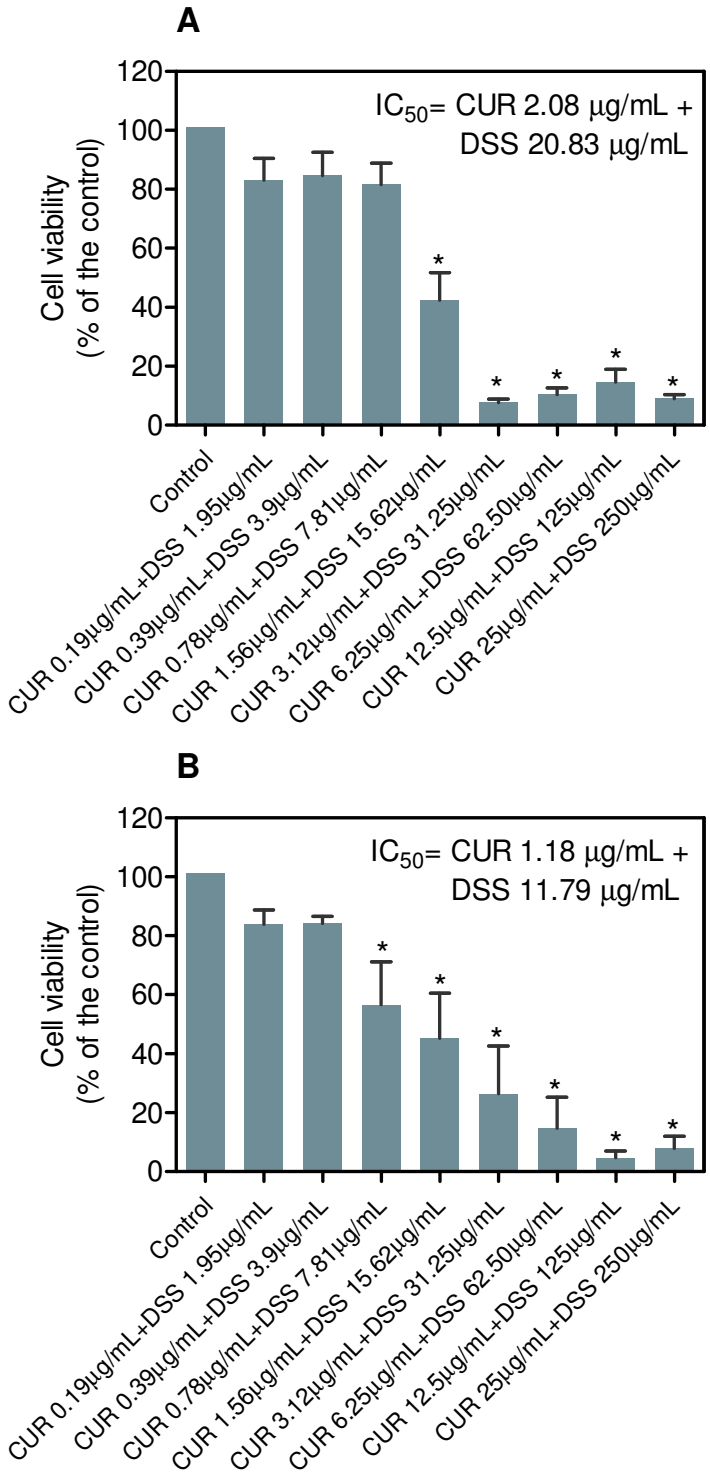

Figure S5. Effect of the combination of CUR and DSS at a ratio of 1:10 on the viability of B16-F10 (**A**) and MRC-5 (**B**) cells measured by the alamar blue method after 72 h of incubation. Data are shown as the mean ± S.E.M. of at least three independent experiments carried out in duplicate. *$P < 0.05$ compared with control (untreated cells) by ANOVA followed by Student Newman–Keuls test.

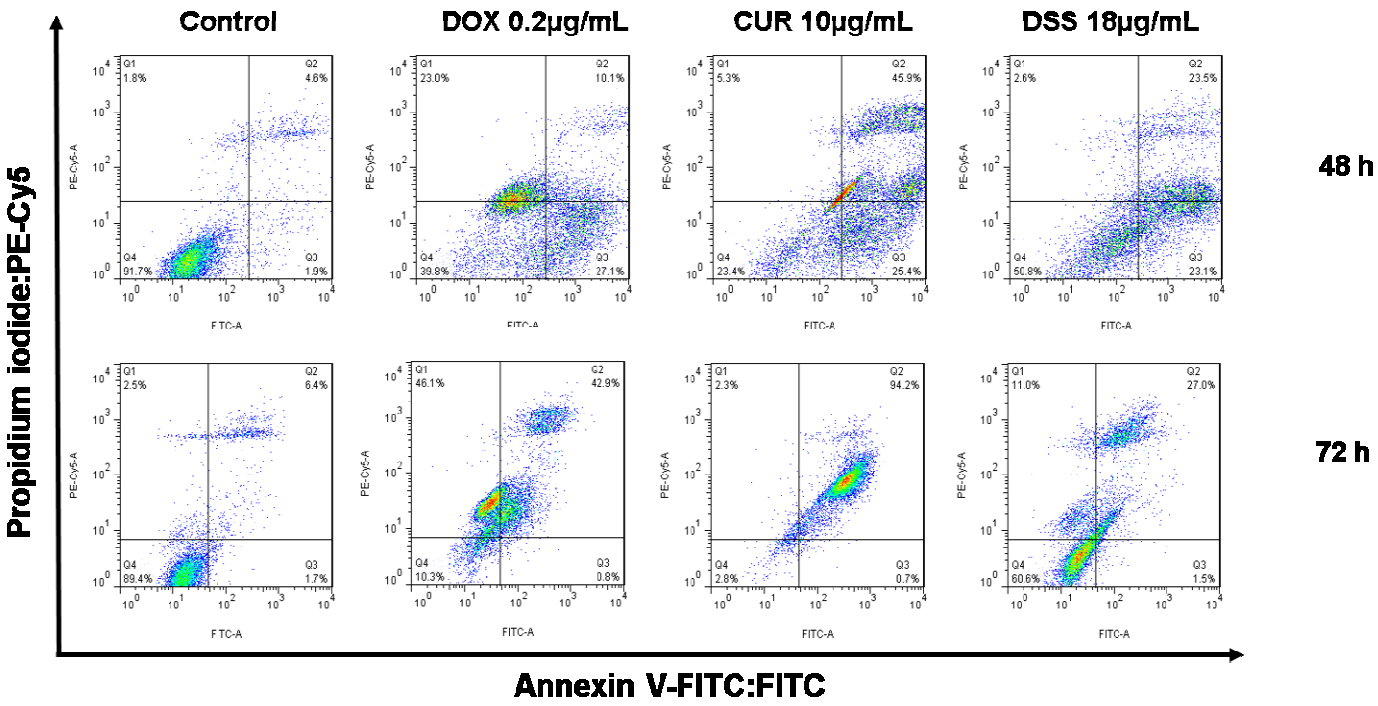

Figure S6. Representative dotplots of the effect of CUR and DSS on the viability of B16-F10 cells measured by annexin V-FITC/PI staining. DOX was used as a positive control, and the negative control received 0.5% DMSO.

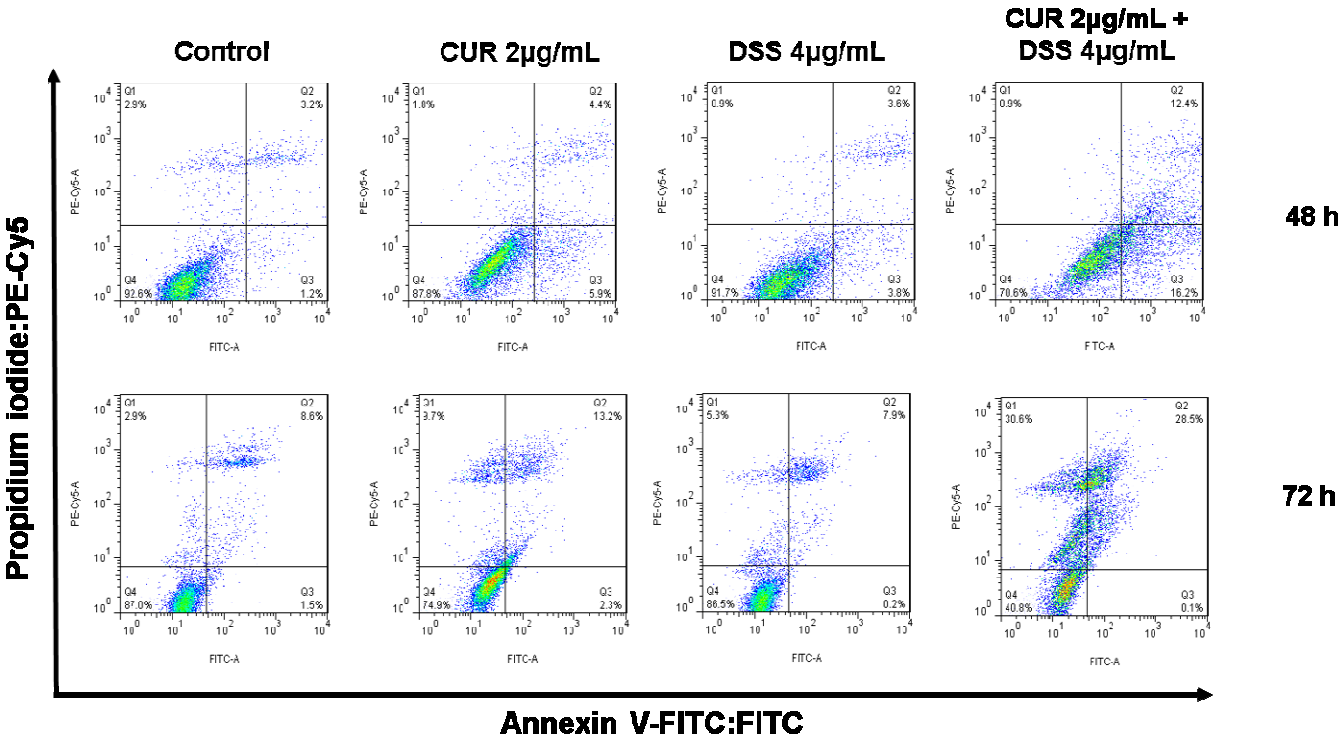

Figure S7. Representative dotplots of the effect of the combination of CUR with DSS at a ratio of 1:2 on the viability of B16-F10 cells measured by annexin V-FITC/PI staining. The control received 0.5% DMSO.

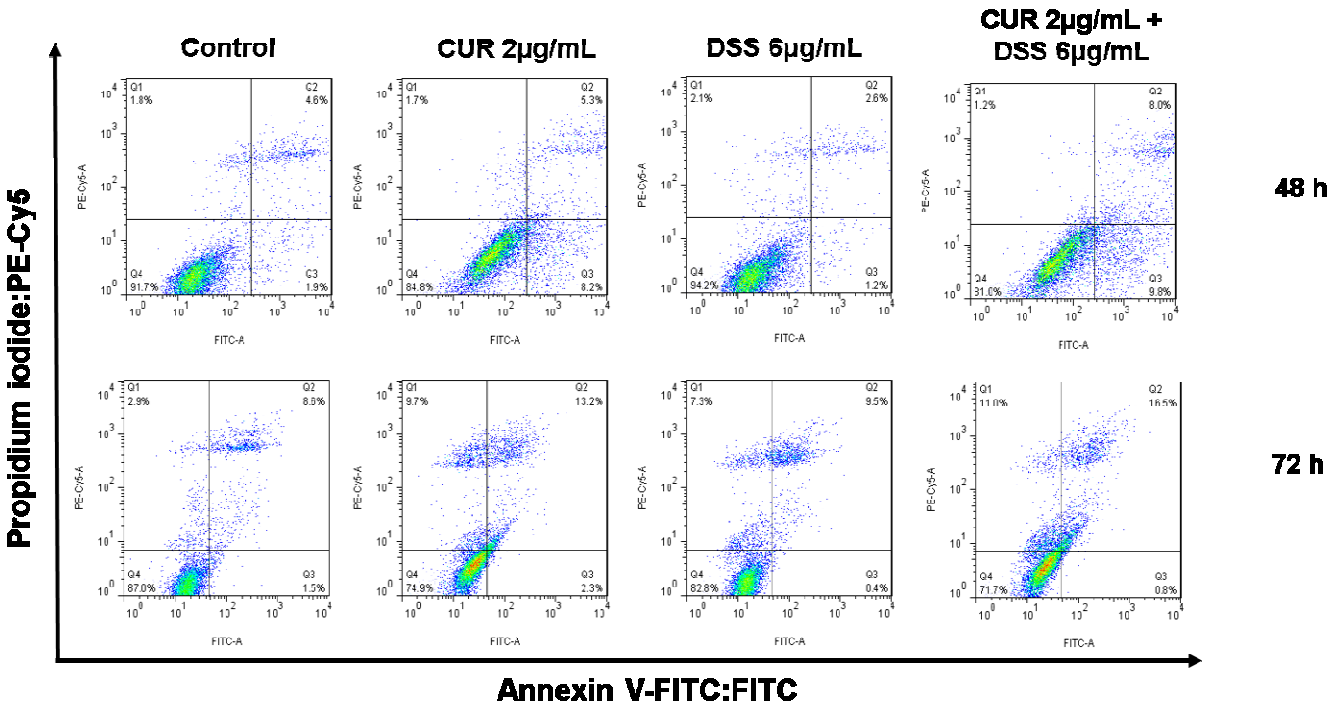

Figure S8. Representative dotplots of the effect of the combination of CUR with DSS at a ratio of 1:3 on the viability of B16-F10 cells measured by annexin V-FITC/PI staining. The control received 0.5% DMSO.

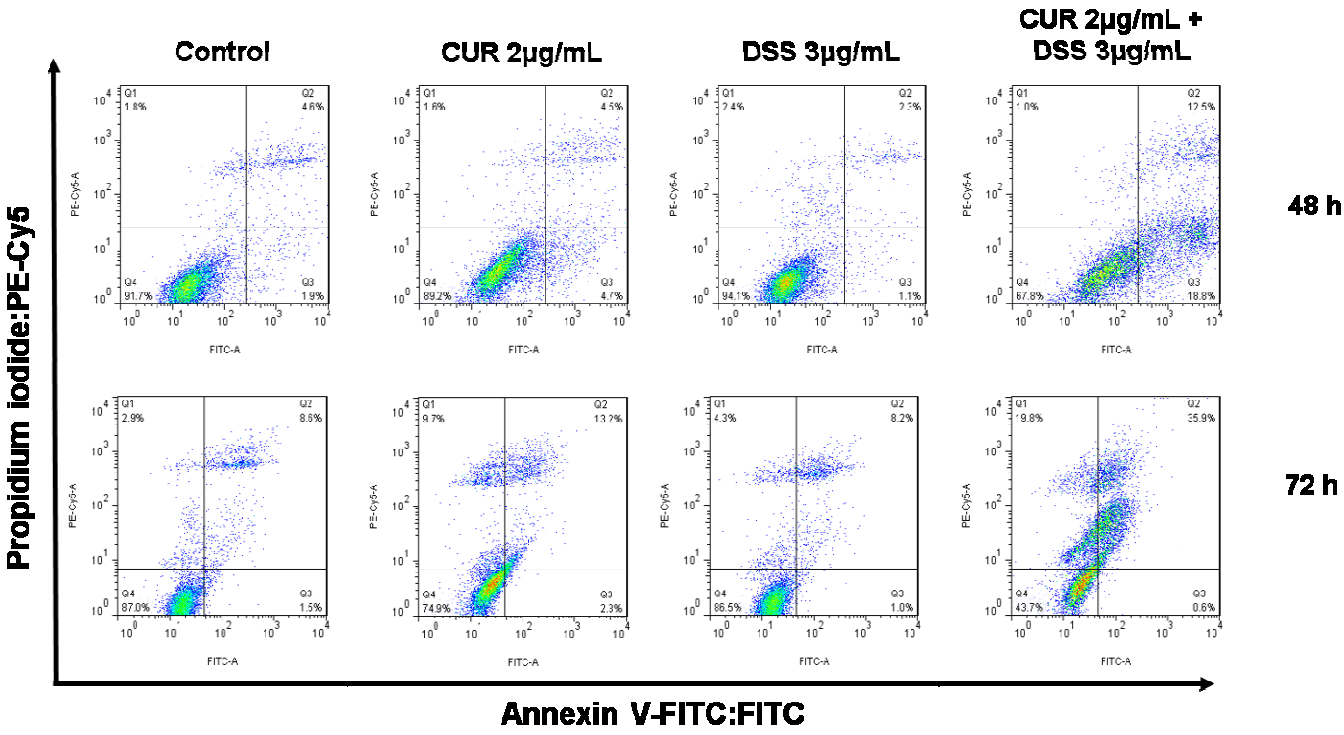

Figure S9. Representative dotplots of the effect of the combination of CUR with DSS at a ratio of 2:3 on the viability of B16-F10 cells measured by annexin V-FITC/PI staining. The control received 0.5% DMSO.

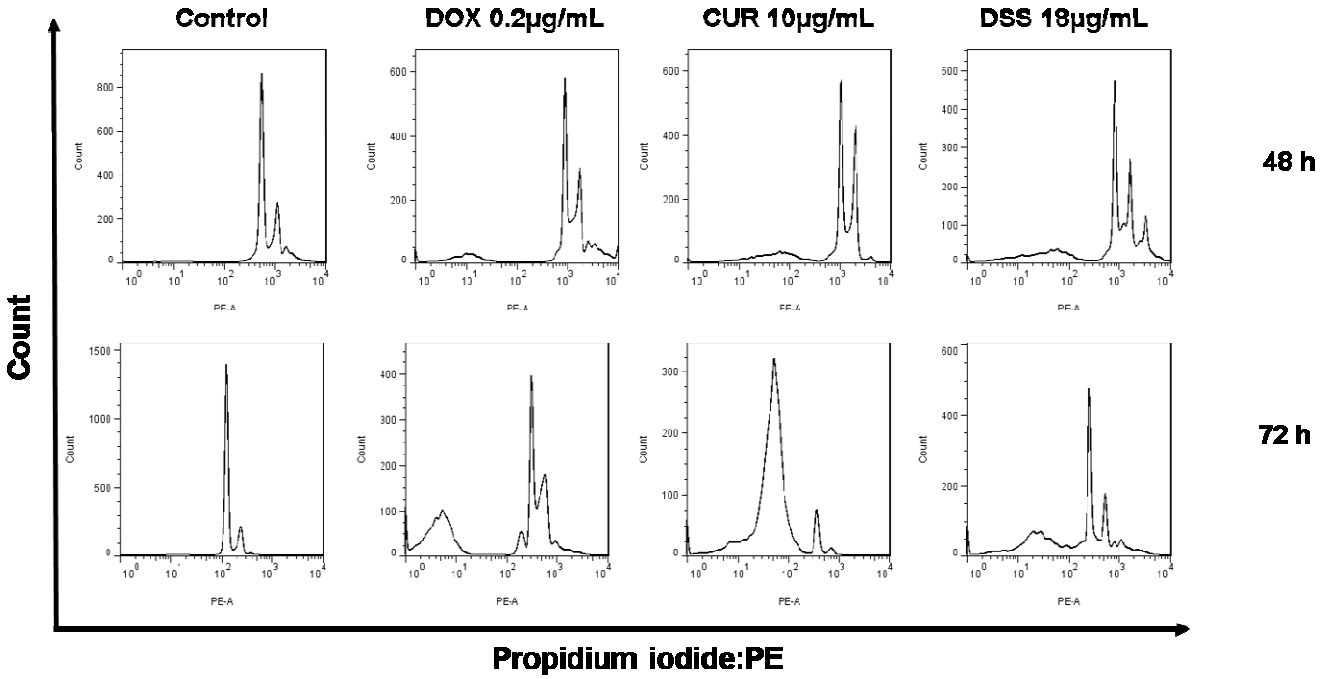

Figure S10. Representative histograms of the effect of CUR and DSS on DNA fragmentation and cell cycle distribution of B16-F10 cells. DOX was used as a positive control, and the negative control received 0.5% DMSO.

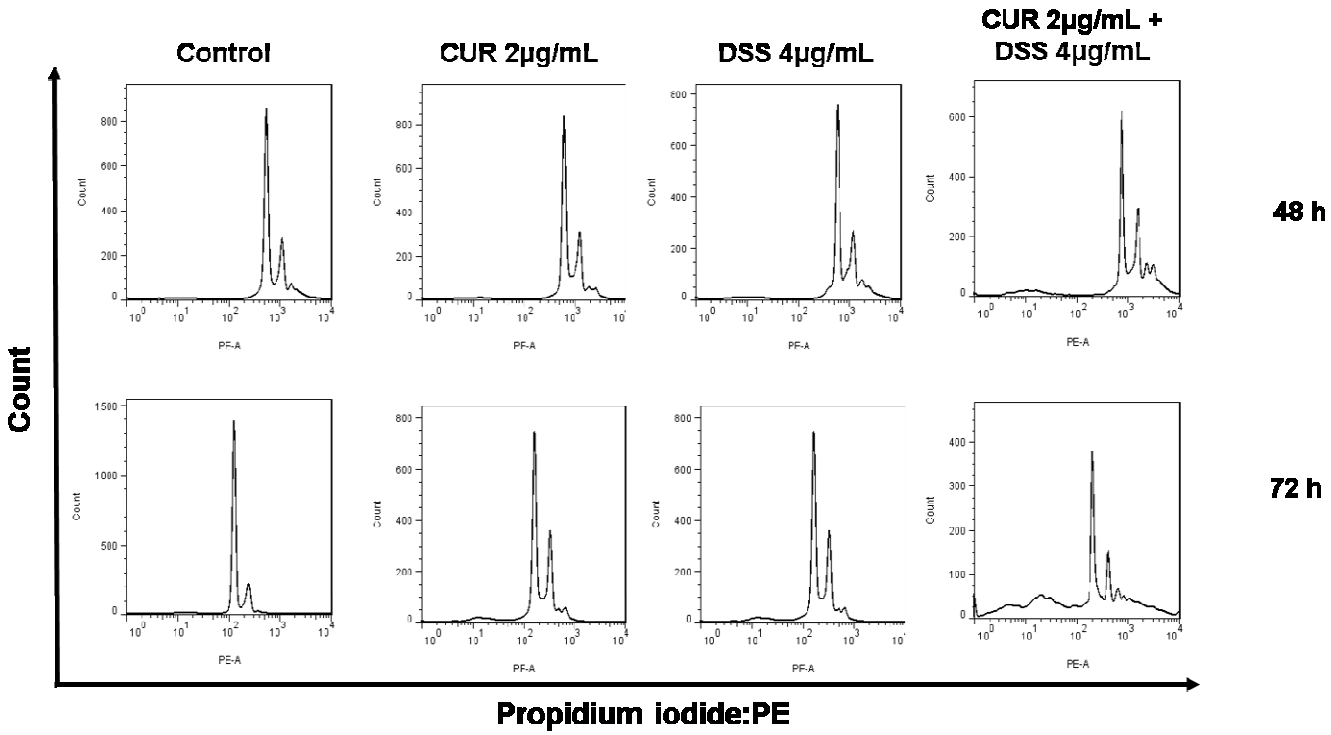

Figure S11. Representative histograms of the effect of the combination of CUR with DSS at a ratio of 1:2 on DNA fragmentation and cell cycle distribution of B16-F10 cells. The control received 0.5% DMSO.

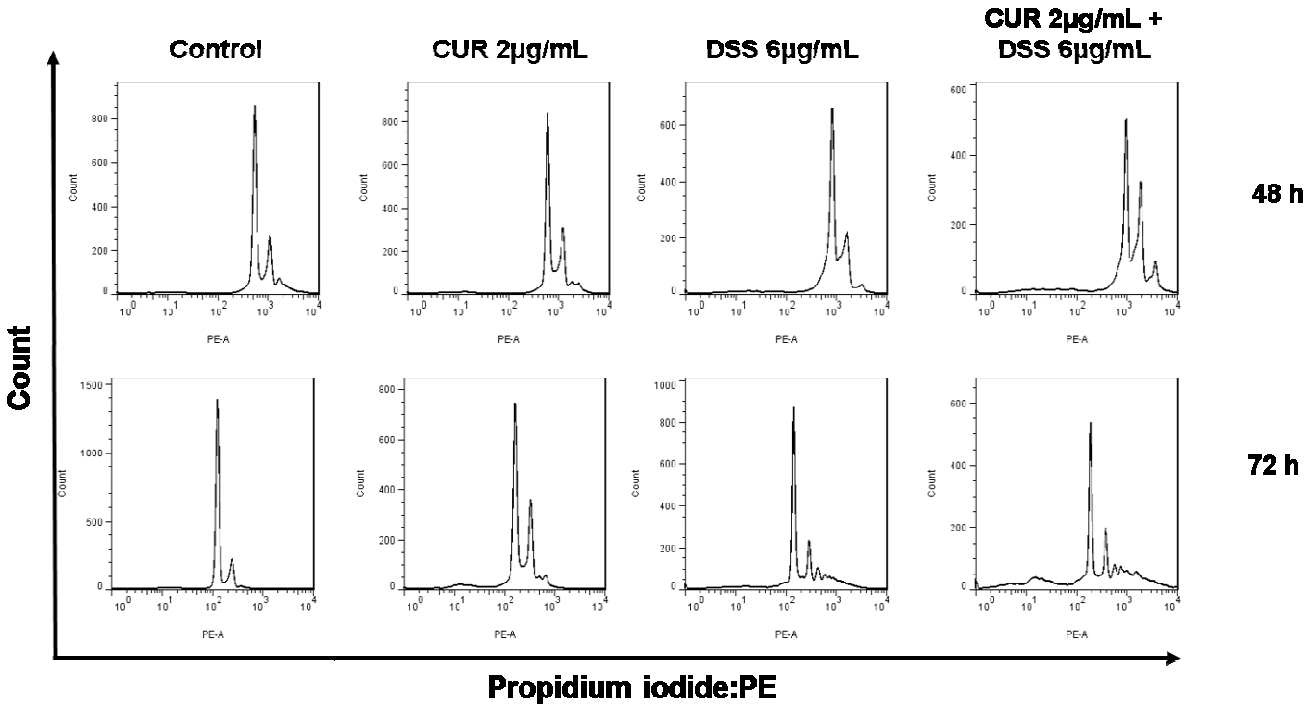

Figure S12. Representative histograms of the effect of the combination of CUR with DSS at a ratio of 1:3 on DNA fragmentation and cell cycle distribution of B16-F10 cells. The control received 0.5% DMSO.

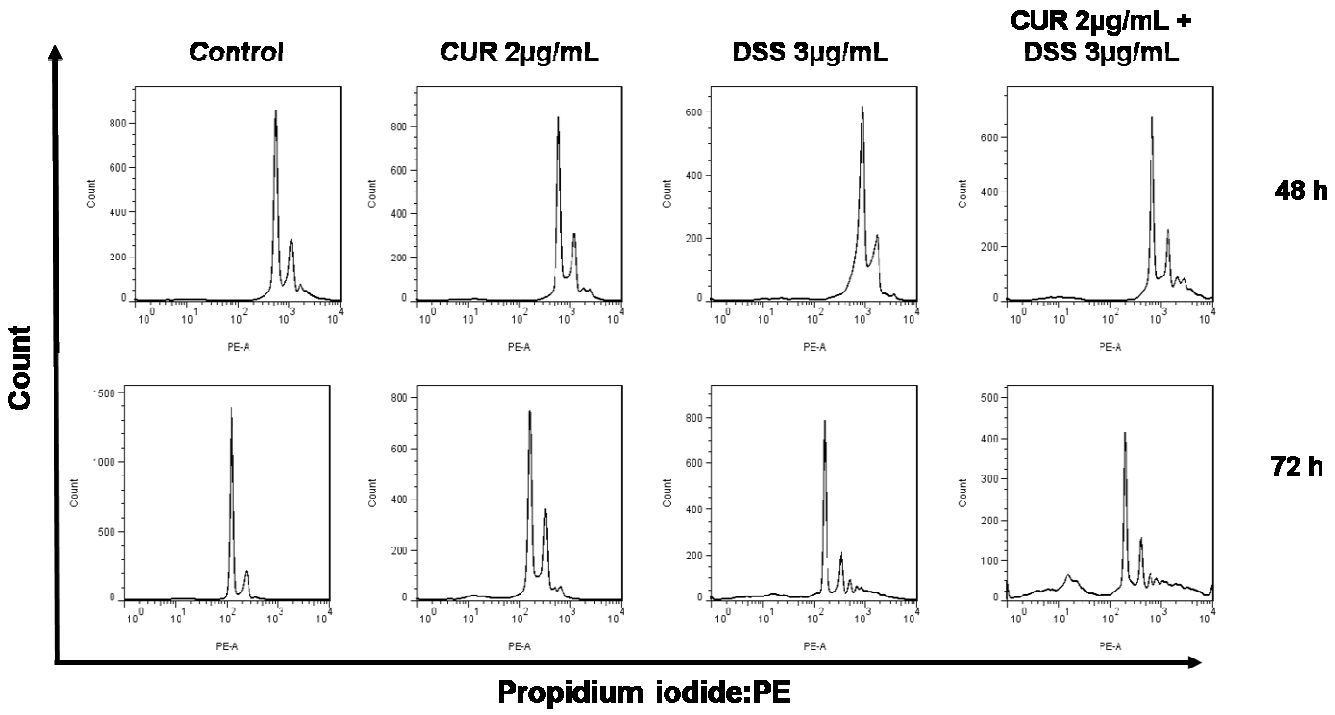

Figure S13. Representative histograms of the effect of the combination of CUR with DSS at a ratio of 2:3 on DNA fragmentation and cell cycle distribution of B16-F10 cells. The control received 0.5% DMSO.

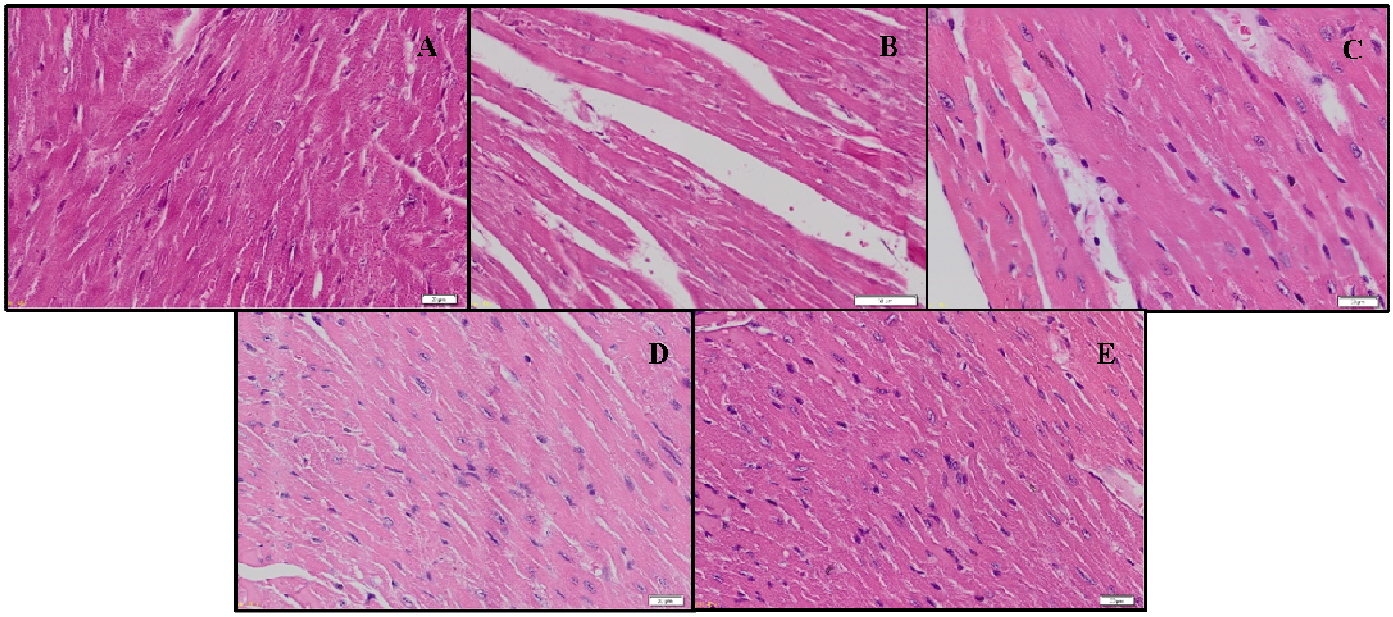

Figure S14. Representative histological analysis of hearts stained with hematoxylin and eosin and analyzed by light microscopy. The animals were treated with 5% DMSO (**A**), 1 mg/kg DOX (**B**), 20 mg/kg CUR (**C**), 60 mg/kg DSS (**D**) or 20 mg/kg CUR + 60 mg/kg DSS (**E**). Intact cardiomyocytes are observed with preservation of nuclei and transverse streaks observed longitudinally. Bars = 20 µm (**A**, **C**, **D** and **E**) or 50 µm (**B**).

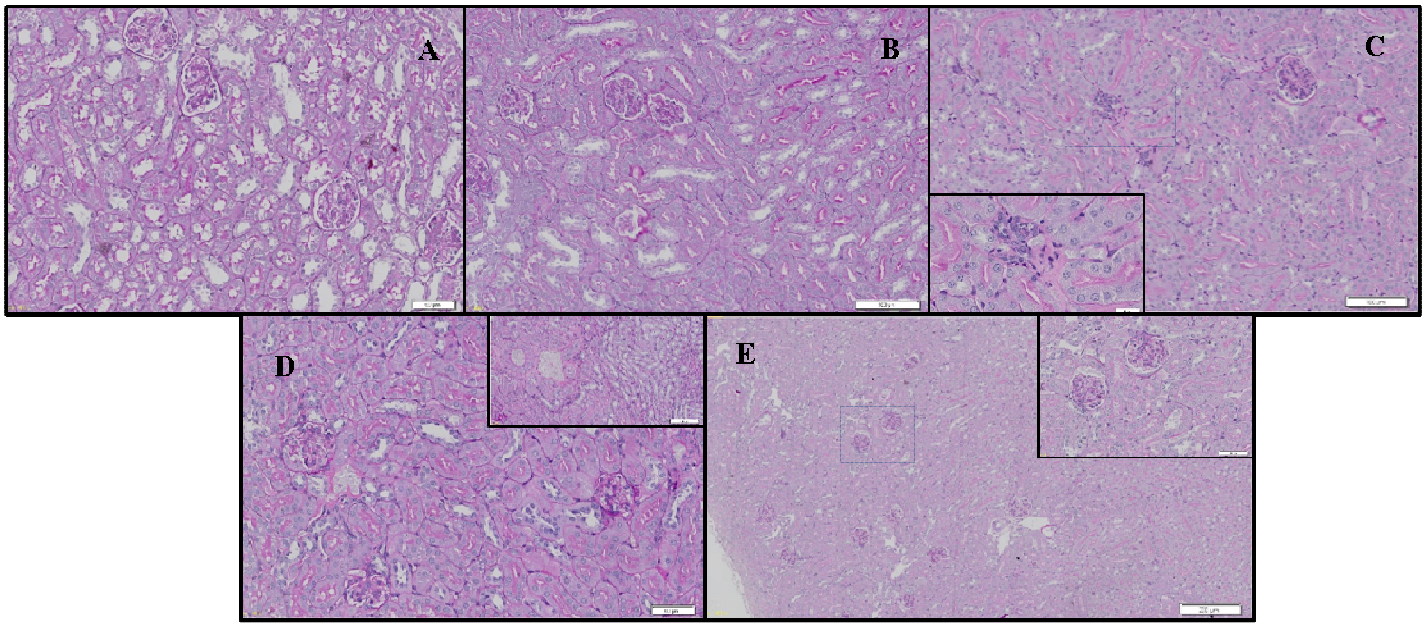

Figure S15. Representative histological analysis of kidneys stained with hematoxylin and eosin and analyzed by light microscopy. The animals were treated with 5% DMSO (**A**), 1 mg/kg DOX (**B**), 20 mg/kg CUR (**C**), 60 mg/kg DSS (**D**) or 20 mg/kg CUR + 60 mg/kg DSS (**E**). Bars = 50 µm (**A** and **D**), 100 µm (**B** and **C**) or 200 µm (**E**).

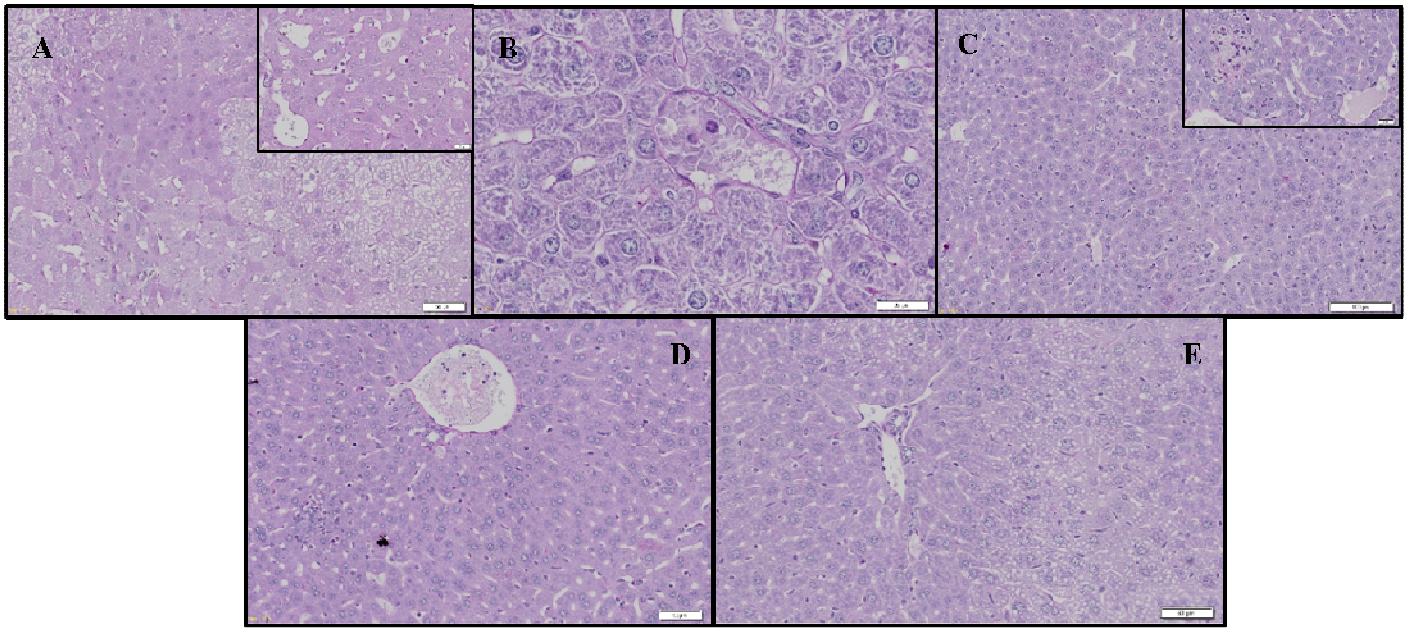

Figure S16. Representative histological analysis of livers stained with hematoxylin and eosin and analyzed by light microscopy. The animals were treated with 5% DMSO (**A**), 1 mg/kg DOX (**B**), 20 mg/kg CUR (**C**), 60 mg/kg DSS (**D**) or 20 mg/kg CUR + 60 mg/kg DSS (**E**). Bars = 50 µm (**A**, **D** and **E**), 20 µm (**B**) or 100 µm (**C**).

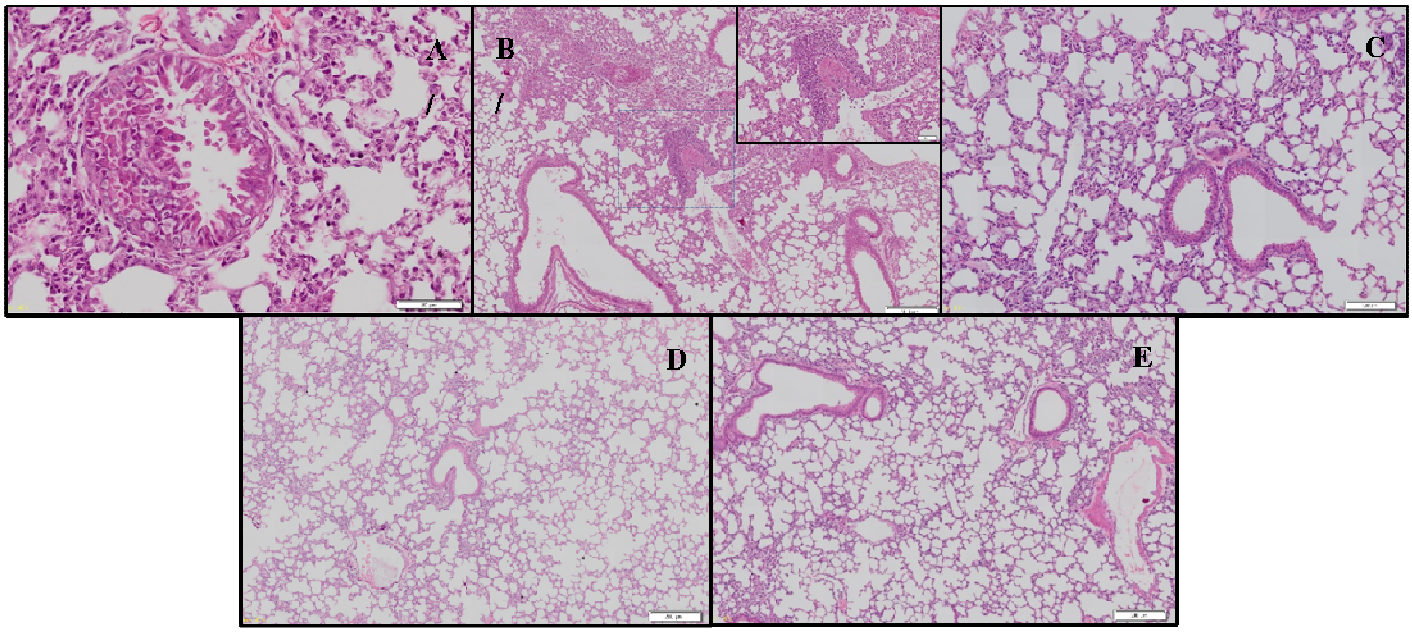

Figure S17. Representative histological analysis of lungs stained with hematoxylin and eosin and analyzed by light microscopy. The animals were treated with 5% DMSO (**A**), 1 mg/kg DOX (**B**), 20 mg/kg CUR (**C**), 60 mg/kg DSS (**D**) or 20 mg/kg CUR + 60 mg/kg DSS (**E**). Bars = 50 µm (**A**), 200 µm (**B**, **D** and **E**) or 100 µm (**C**).

Table S1. Inhibitory concentrations of CUR and DSS alone and in combination.

	Inhibitory effect	CUR combinated (µg/mL)	CUR alone (µg/mL)	FIC of CUR	DSS combinated (µg/mL)	DSS alone (µg/mL)	FIC of DSS
Ratio 1:2	25%	8.11	7.69	1.05	16.49	14.80	1.11
	50%	1.79	9.69	0.18	3.98	16.49	0.24
	75%	16.21	13.70	1.18	32.28	21.47	1.50
Ratio 1:3	25%	6.47	7.69	0.84	19.43	14.80	1.31
	50%	2.76	9.69	0.28	8.30	16.49	0.50
	75%	8.62	13.70	0.63	25.87	21.47	1.20
Ratio 1:4	25%	4.35	7.69	0.57	17.43	14.80	1.18
	50%	3.74	9.69	0.39	15.00	16.49	0.91
	75%	7.09	13.70	0.52	28.38	21.47	1.32
Ratio 2:3	25%	8.34	7.69	1.08	11.61	14.80	0.78
	50%	1.96	9.69	0.20	3.18	16.49	0.19
	75%	13.67	13.70	1.00	20.63	21.47	0.96
Ratio 1:10	25%	1.57	7.69	0.20	15.80	14.80	1.07
	50%	2.08	9.69	0.21	20.83	16.49	1.26
	75%	2.46	13.70	0.18	24.71	21.47	1.15

Table S2. Effect of CUR and DSS and their combination on body and relative organ weight from C57BL/6 mice bearing B16-F10 cells.

	Control	**DOX**	**CUR**	**DSS**	**CUR + DSS**
Dose (mg/kg)	-	1	20	60	20 + 60
Survival	10/10	09/10	09/10	09/10	07/10
Initial body weight (g)	21.60 ± 1.2	27.83 ± 0.4	25.65 ± 0.8	26.05 ± 0.6	23.23 ± 1.1
Final body weight (g)	26.83 ± 1.8	31.89 ± 0.9	29.89 ± 0.9	28.56 ± 0.8	26.71 ± 2.2
Heart (g/100 g body weight)	0.56 ± 0.05	0.39 ± 0.02	0.40 ± 0.01	0.69 ± 0.31	0.40 ± 0.05
Liver (g/100 g body weight)	5.42 ± 0.6	4.14 ± 0.2	4.06 ± 0.1	3.88 ± 0.2	4.21 ± 0.8
Lung (g/100 g body weight)	0.68 ± 0.07	0.51 ± 0.02	0.56 ± 0.06	0.57 ± 0.02	0.56 ± 0.07
Kidneys (g/100 g body weight)	1.27 ± 0.1	0.92 ± 0.04	1.01 ± 0.06	1.01 ± 0.04	1.03 ± 0.2

DOX was used as a positive control, and the negative control received 5% DMSO. Data are shown as the mean ± S.E.M. of 7-10 animals.

Table S3. Effect of CUR and DSS and their combination on hematological parameters of peripheral blood from C57BL/6 mice bearing B16-F10 cells

	Control	**DOX**	**CUR**	**DSS**	**CUR + DSS**
Dose (mg/kg)	-	1	20	60	20 + 60
Erythrocytes (10^6/mm^3)	5.8 ± 0.7	8.5 ±0.4*	7.0 ± 0.7	9.0 ± 0.3**	6.7 ± 0.6
Hemoglobin (g/dL)	10.2 ± 1.2	14.4 ± 0.9*	12.4 ± 1.0	14.8 ± 0.4*	12.6 ± 0.9
Hematocrit (%)	35.4 ± 4.5	47.7 ± 2.9	43.7 ± 4.2	49.6 ± 1.1	36.6 ± 6.5
MCV (fL)	63.8 ± 1.6	54.3 ± 1.5*	61.9 ± 2.4	59.9 ± 1.5	60.6 ± 1.7
Platelets (10^3/mm^3)	55 ± 13	287 ± 77*	83,3 ± 14	120 ± 40	188 ± 88
Leukocytes (10^3/mm^3)	3.5 ± 0.6	3.1 ± 0.5	2.6 ± 0.4	5.5 ± 0.6	4.6 ± 0.8
Contagem diferencial de leucócitos (%)					
Lymphocytes	53.4 ± 5.7	48.9 ± 3.6	63.5 ± 5.7	47.5 ± 4.9	51.4 ± 3.3
Monocytes	28.2 ± 2.2	24.8 ± 2.8	22.0 ± 2.9	34.2 ± 2.3	32.7 ± 2.1
Granulocytes	18.4 ± 5.3	26.3 ± 2.1	26.7 ± 12.5	18.2 ± 3.4	16.0 ± 3.3

DOX was used as a positive control. Data are shown as the mean ± S.E.M. of 7-10 animals. *$p < 0.05$ compared with control (5% DMSO) by ANOVA followed by Student Newman–Keuls test. MCV: Mean corpuscular volume.