Data S1: Supplementary methods used

Qualitative analysis of Coptis chinensis extract by ultra-performance liquid chromatography (UPLC)-quadrupole time-of-flight (QTOF). Chromatographic analysis of the extract was performed to identify and provide chemical components to qualify and identify the origin of *Coptis chinensis* authentically. Approximately 20 mg of the extract power were shaken with 1 ml of 70% ethanol by a vortex mixer for 30 sec The supernatants were filtered through a 0.2-μm polytetrafluoroethylene syringe filter (Thermo Fisher Scientific, Inc.). Finally, the filtrate was diluted in a final concentration 100 μg/ml and transferred to a LC sample vial prior to use. The liquid chromatography-mass spectrometry system consisted of a Thermo Scientific Vanquish UHPLC system (Thermo Fisher Scientific, Inc.) with an ACQUTY UPLC HSS T3 column (2.1x100 mm, 1.8 μm; Waters) and a Triple TOF5600$^+$ mass spectrometer system (Triple TOF MS; QTOF, SCIEX). The QTOF MS, equipped with a Duospray™ ion source, was used to complete the high-resolution experiment. The analysis method was described in a previous study (1). Data acquisition and processing for qualitative analysis were carried out using Analyst TF 1.7, PeakVeiw2.2 and MasterView (SCIEX).

MTT assay with berberine. Cell viability was measured by MTT assay. Briefly, 1x10^3 cells per well were seeded in 96-well culture plates overnight and, subsequently incubated for 72 h at 37˚C without (DMSO) or with the relevant concentration (0, 1, 5, 10, 20 and 50 μM) treatments of berberine. After 72 h, 50 μl MTT solution (0.5 mg/ml, Sigma-Aldrich; Merck KGaA) were added to each well. Following incubation at 37˚C for a further 4 h, the MTT solution was discarded and DMSO was added. The absorbance at 750 nm was measured using a microplate reader (SpectraMax Plus 384, Molecular Devices, LLC).

HCC827GRAMC$^+$ cell line. The gefitinib-resistant cell line, HCC827GRAMC, was a gift from Dr J.K. Rho, Ulsan University, Asan Hospital. This cell line is a gefitinib-resistant cell line with a resistant mechanism which different from that of the HCC827GRKU cells. The HCC827GRKU cells have an acquired KEPA1 mutation (2), whereas the HCC827GRAMC$^+$ cells have an acquired MET activation (3). This cell line was only used in the experiment presented in Fig. S3.

References

1. Oh JH, Ha IJ, Lee MY, Kim EO, Park D, Lee JH, Lee SG, Kim DW, Lee TH, Lee EJ, *et al*: Identification and metabolite profiling of alkaloids in aerial parts of *Papaver rhoeas* by liquid chromatography coupled with quadrupole time-of-flight tandem mass spectrometry. J Sep Sci 41: 2517-2527, 2018.
2. Park SH, Kim JH, Ko E, Kim JY, Park MJ, Kim MJ, Seo H, Li S and Lee JY: Resistance to gefitinib and cross-resistance to irreversible EGFR-TKIs mediated by disruption of the Keap1-Nrf2 pathway in human lung cancer cells. FASEB J 32: 5862-5873, 2018.
3. Rho JK, Choi YJ, Kim SY, Kim TW, Choi EK, Yoon SJ, Park BM, Park E, Bae JH, Choi CM and Lee JC: MET and AXL inhibitor NPS-1034 exerts efficacy against lung cancer cells resistant to EGFR kinase inhibitors because of MET or AXL activation. Cancer Res 74: 253-262, 2014.

Figure S1. Identification of chemical components in ECC. UPLC-QTOF analysis conducted to determine the chemical profile and identify the major constituents from ECC. Representative (A) Base peak chromatogram (BPC) of ECC, (B) extracted ion chromatogram (XIC) of representative components in ECC, and (C) extracted ion chromatogram (XIC) of mixed standard compounds were obtained by UPLC-QTOF analysis in positive ion mode: 1, jatrorrhizine; 2, columbamin; 3, epi-berberine; 4, coptisine; 5, palmatine; 6, berberine. ECC, extract of *Coptis chinensis*; UPLC-QTOF, ultra-performance liquid chromatography-quadrupole time-of-flight.

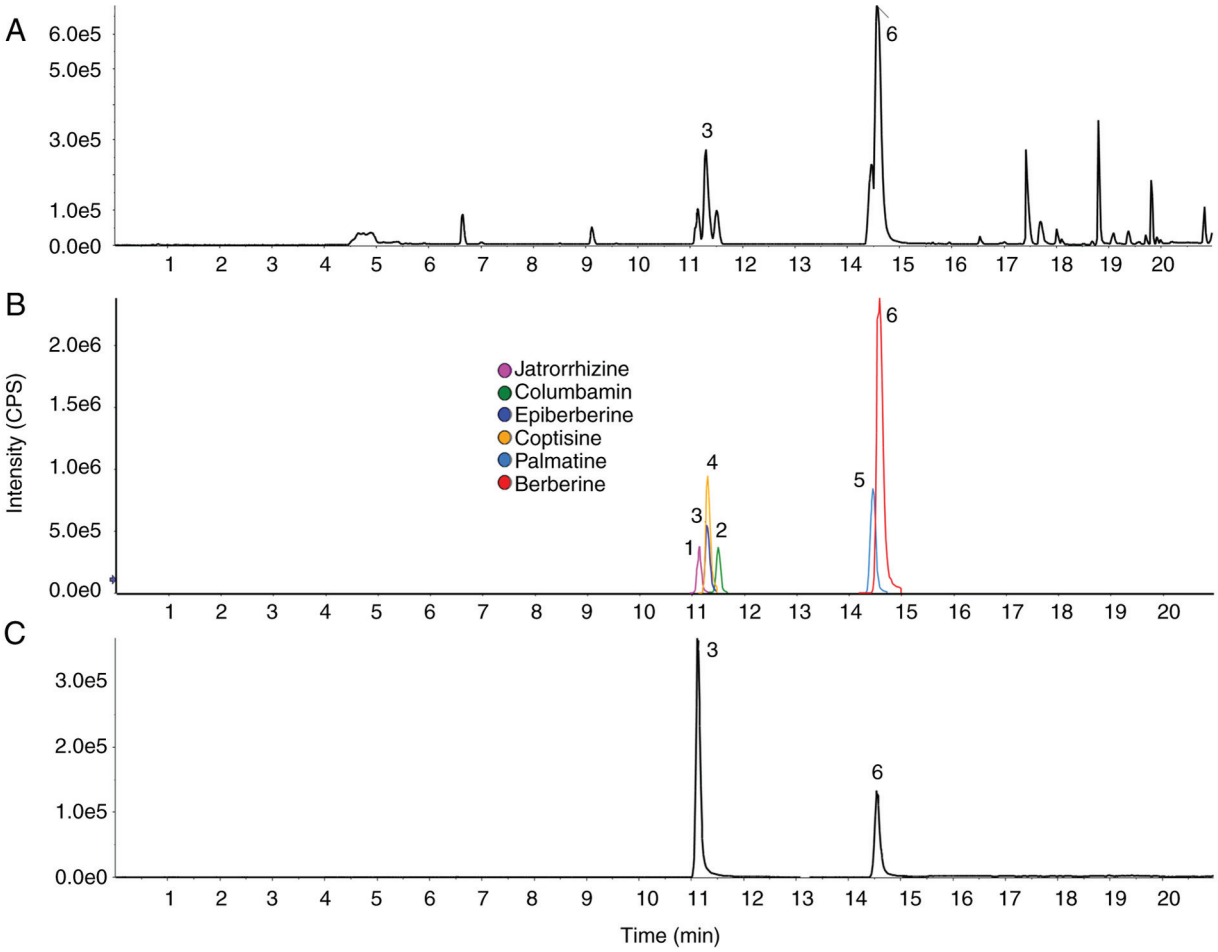

Figure S2. Berberine was shown to exert cytotoxic effects on lung cancer cells, as well as on normal BEAS-2B cells, as determined by MTT assay. It should be noted that berberine also exerted significant cytotoxic effects on the BEAS-2B cells. This significance ($P<0.05$) is not indicated in the figure however, due to space limitations. The results are shown as the means ± SD of triplicate experiments. $^{*}P<0.05$, and $^{***}P<0.001$; the hash symbol (#) indicates that there were no significant differences.

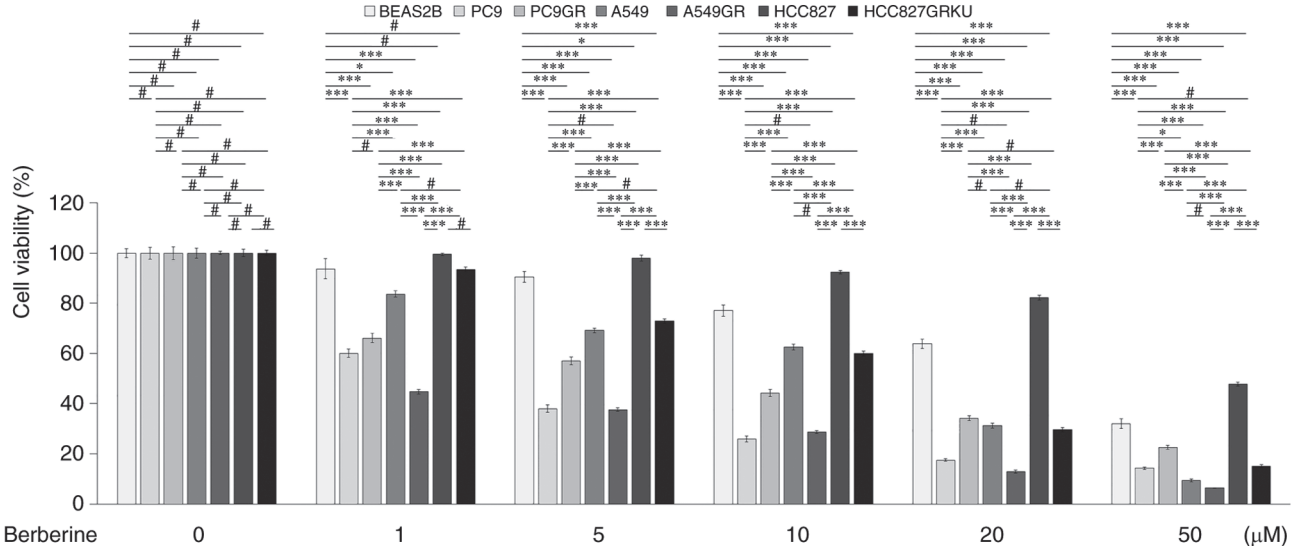

Figure S3. ECC suppresses the anti-apoptotic proteins, Bcl-2 and Mcl-1, in HCC827GRKU cells. (A) Bcl-2 and Mcl-2 were overexpressed in HCC827GRKU cells compared with parental cells, as determined by western blot analysis. The suppression of Bcl-2 and Mcl-1 by ECC was examined by (B) western blot analysis and (C) RT-qPCR. The results shown are the means ± SD of triplicate experiments. $^{***}P<0.001$. HCC827GRAMC^{+} is a gefitinib-resistant cell with a different resistant mechanism (this cell line was only used in this experiment). ECC, extract of *Coptis chinensis*; GR, gefitinib-resistant.

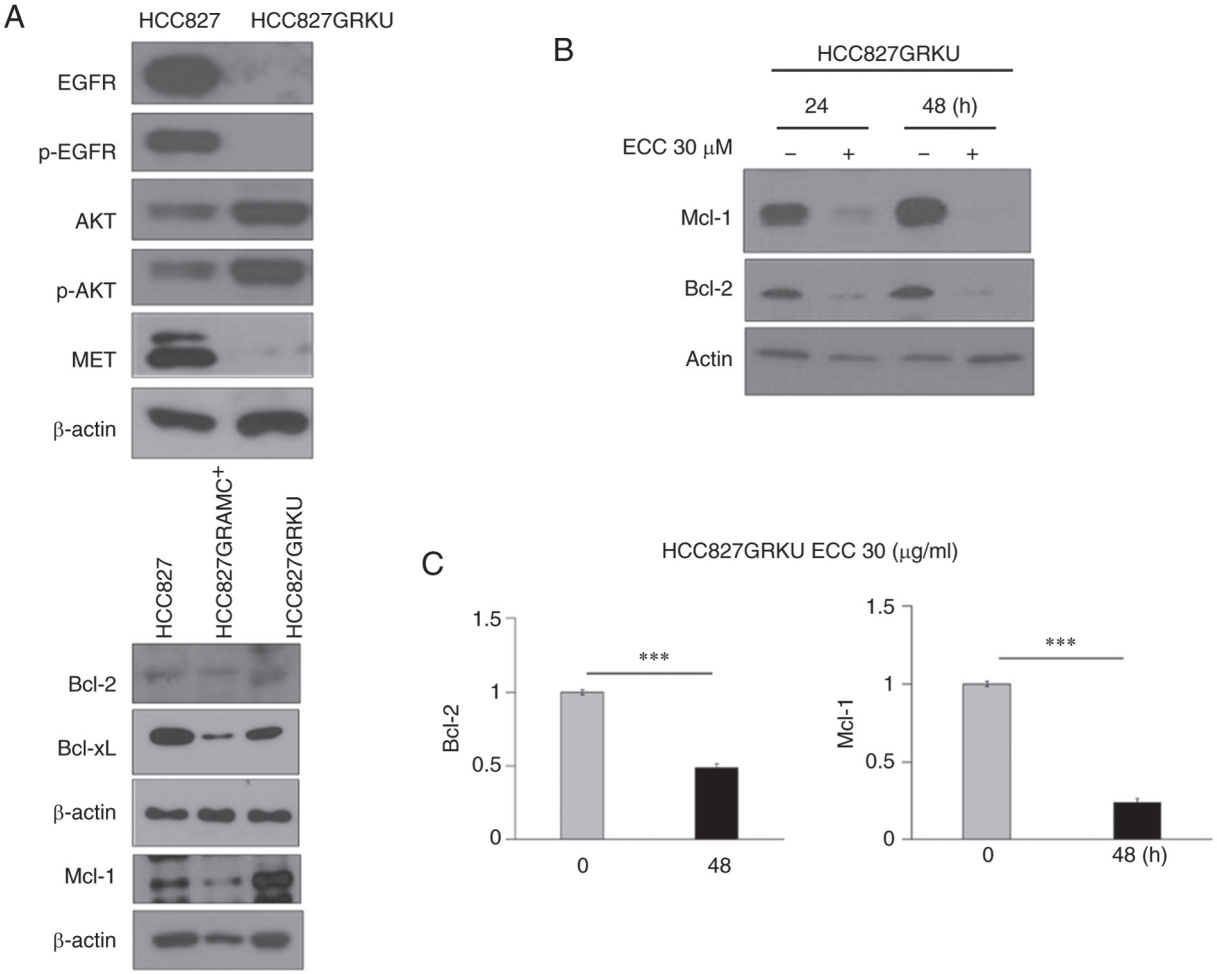

Table SI. Identification of chemical components authentically or tentatively in *Coptis chinensis* extract.

Name	Formula	Mass (Da)	Adduct	Found at mass (Da)	Error (ppm)	Expected RT (min)
Jatrorrhizine	$C_{20}H_{20}NO_4$	338.1392	$[M]^+$	338.1390	0.8	11.14
Columbamin	$C_{20}H_{20}NO_4$	338.1392	$[M]^+$	338.1389	0.7	11.50
Epiberberine	$C_{20}H_{18}NO_4$	336.1236	$[M]^+$	336.1231	0.2	11.29
Coptisine	$C_{19}H_{14}NO_4$	320.0923	$[M]^+$	320.0919	0.4	11.30
Palmatine	$C_{21}H_{22}NO_4$	352.1549	$[M]^+$	352.1546	0.8	14.45
Berberine	$C_{20}H_{18}NO_4$	336.1236	$[M]^+$	336.1233	0.8	14.58