

Supplementary figures for:

Cannabidiol enhances cabozantinib-induced apoptotic cell death via phosphorylation of p53 regulated by ER stress in hepatocellular carcinoma

Authors: Youngsic Jeon^{1,†}, Taejung Kim^{1,2,†}, Hyukjoon Kwon¹, Jeong Kook Kim³, Young-Tae Park¹, Jungyeob Ham^{1,2,3,*} and Young-Joo Kim^{1,*}

Author Affiliations:

¹ Natural Products Research Center, Korea Institute of Science and Technology, Gangneung, Republic of Korea

² Division of Bio-Medical Science & Technology, KIST School, University of Science and Technology, Seoul 02792, Republic of Korea,

³ NeoCannBio Co., Ltd., Seoul, Republic of Korea

Supplementary Figures

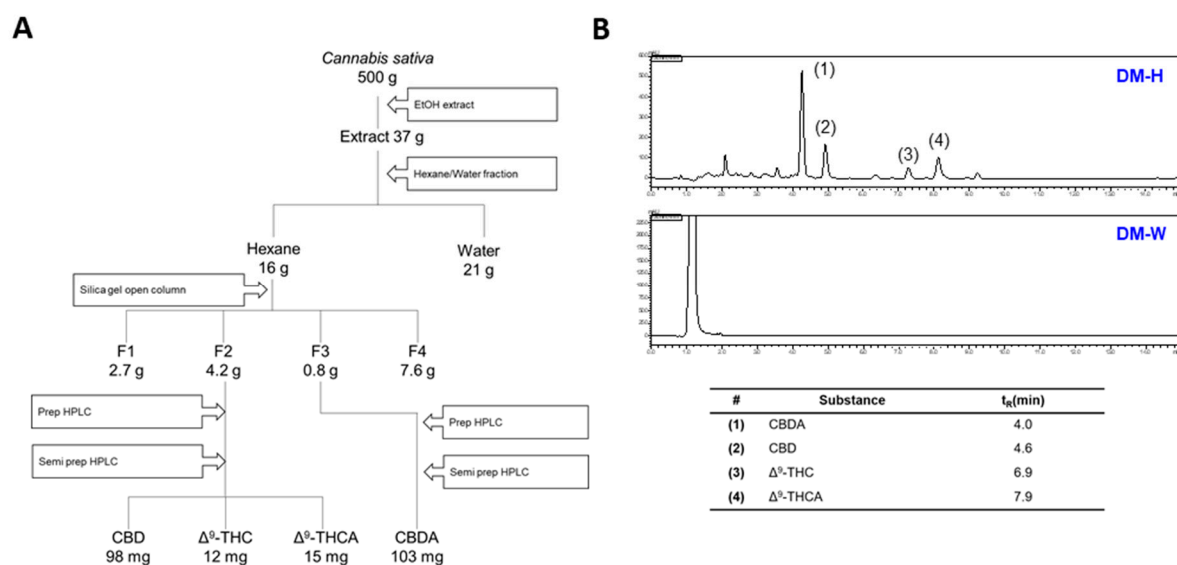


Figure S1. Most abundant compounds of cannabis plants. **(A)** The chemical structure of cannabinoids of *Cannabis sativa*. **(B)** High-performance liquid chromatography (HPLC) of ethanolic extracts and separated cannabinoids. **(B)** Extraction and isolation of cannabinoids. CBDA: Cannabidiolic acid, CBD: Cannabidiol, Δ^9 -THC: Tetrahydrocannabinol, Δ^9 -THCA: Tetrahydrocannabinolic acid.

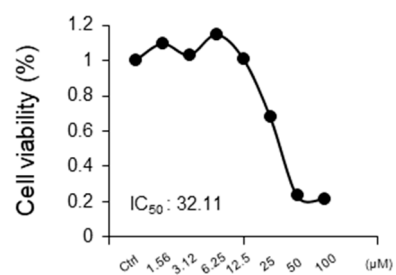


Figure S2. Cell viability of cabozantinib and CBD combination treatment in Hep3B. Cytotoxicity mediated by cabozantinib and CBD was assessed using the WST-8 assay in Hep3B.

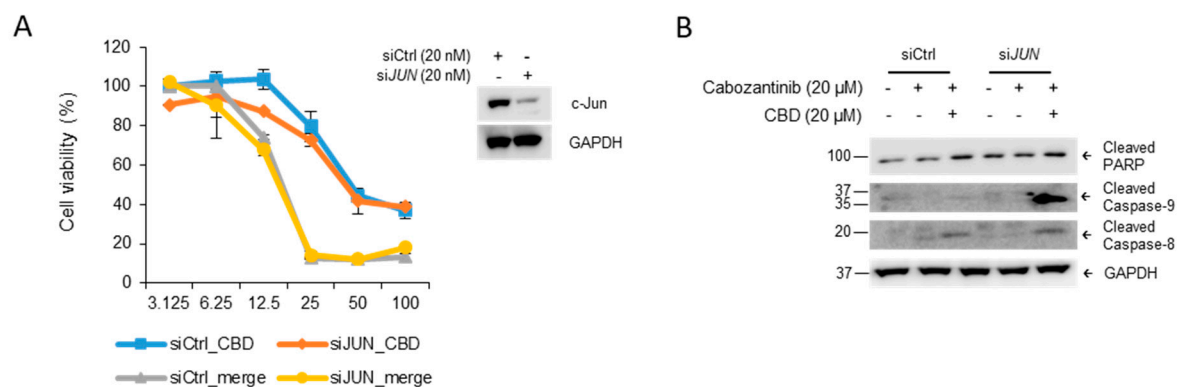


Figure S3. The effect of JUN knock-down on apoptosis after the combination treatment. **(A)** *JUN* siRNA (20 nM) and control siRNA (20 nM) were used to transfect HepG2 cells for 48 h; cytotoxicity induced by cabozantinib with and without CBD was assessed using WST-8 assay (*left*) and western blotting (*right*) at different concentrations. **(B)** *JUN* siRNA (20 nM) and control siRNA (20 nM) were used to transfect HepG2 cells, and the levels of apoptosis-related proteins (PARP, cleaved caspase-9, and cleaved caspase-8) were assessed using western blotting. Protein levels were normalized to those of GAPDH.

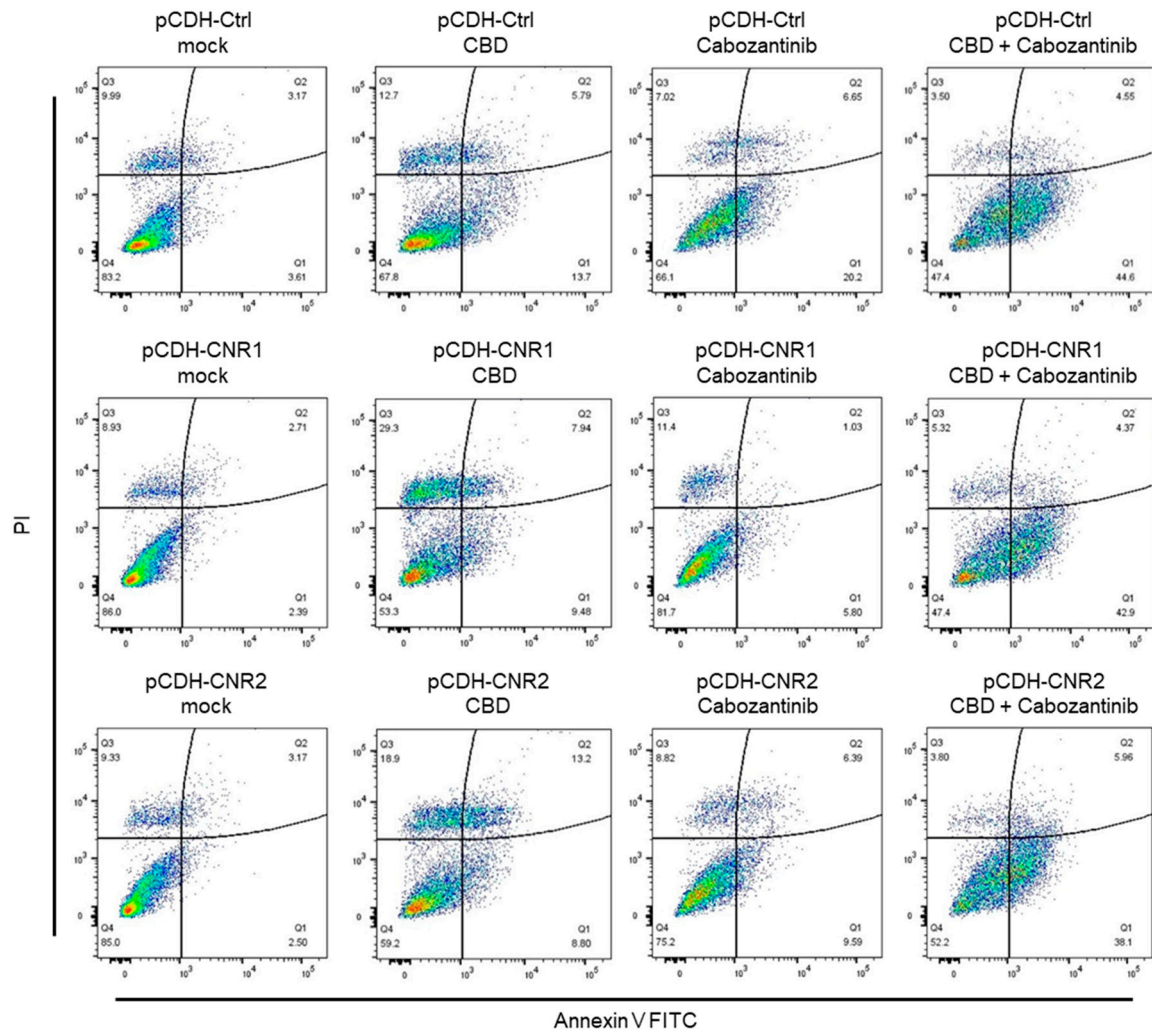


Figure S4. The effect of combination treatment in *CNR1* and *CNR2* stable cell lines. Fluorescence-activated cell sorting analysis of early apoptosis in stable cell lines incubated at the indicated condition.