Supplementary Materials

Betulin, a newly characterized compound in *Acacia auriculiformis* bark, is a multi-target protein kinase inhibitor

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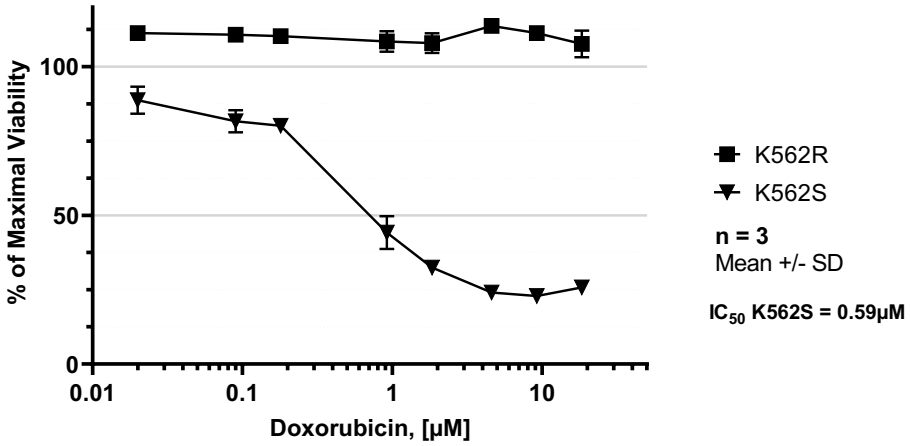

Figure S1. *In vitro* effect of doxorubicin on the cell viability of K562 chronic myelogenous leukemia (CML) cells. The viability of K562S and K562R CML cell lines, that are respectively sensitive (S) and resistant (R) to treatment with doxorubicin, was studied by using the MTS assay. Cell viability was measured after 48-hours exposure to increasing doses of doxorubicin. The IC_{50} value was determined from the dose-response curve using GraphPad PRISM Software. Data are mean (n=3) ± SD expressed in % of maximal viability (cells treated with a similar dose of DMSO).

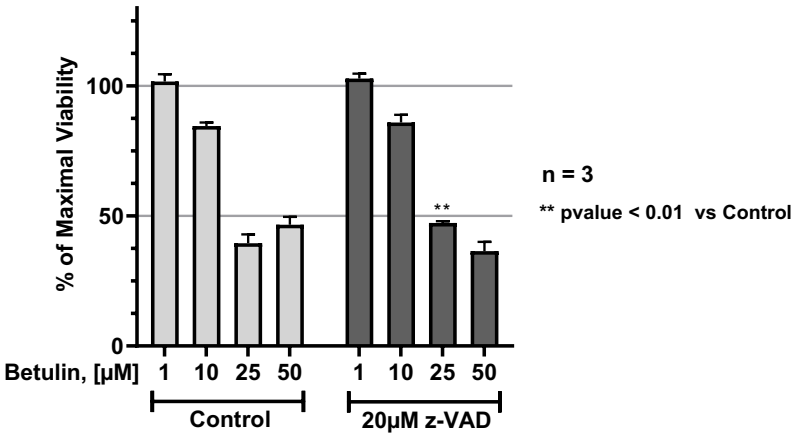

Figure S2. The effect of treatment with pan caspase inhibitor z-VAD-fmk on the phenotype induced by betulin. The viability of K562S CML cell line was studied by using the MTS assay. Cell viability was studied after 48-hours exposure of increasing doses of betulin (from 1 to 50µM) alone or co-treated with 20µM of z-VAD-fmk. Data are mean (n=3) ± SD expressed in % of maximal viability (cells treated with a similar dose of DMSO). ** $p < 0.01$ vs control.

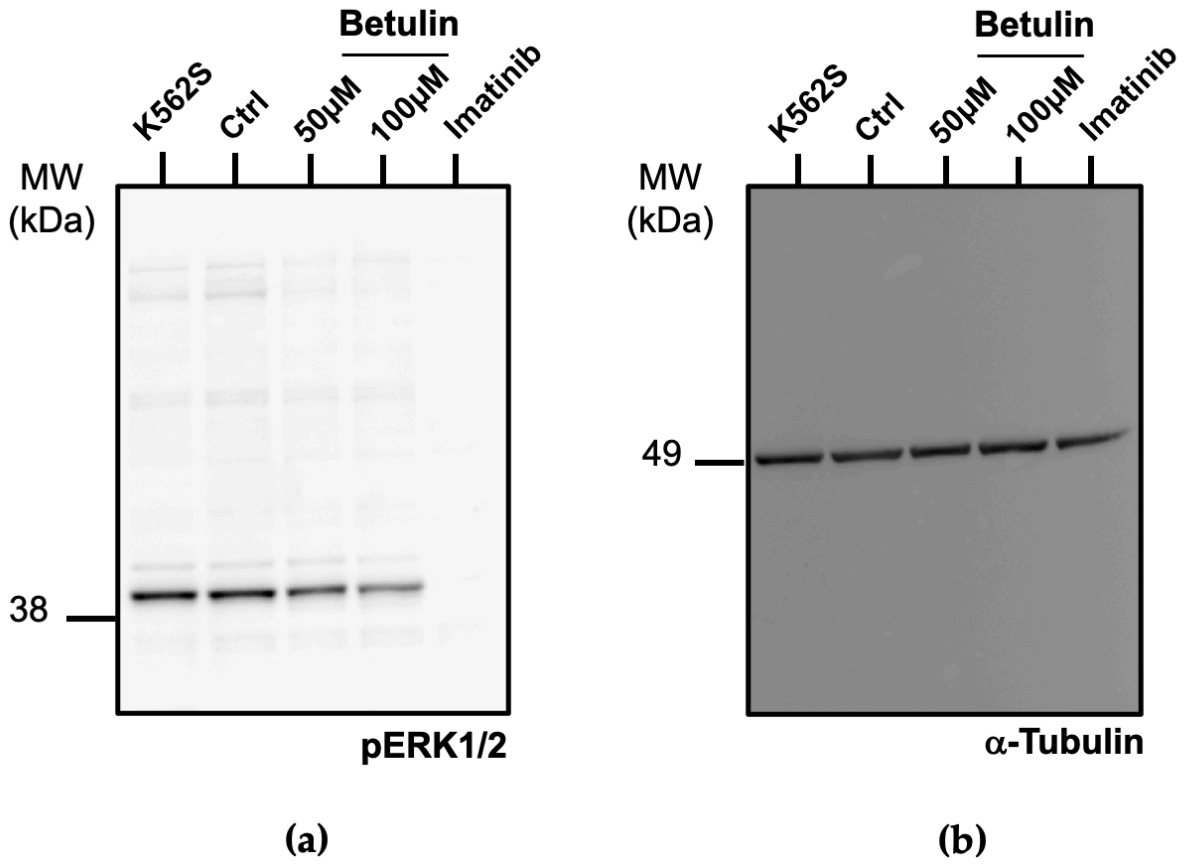

Figure S3. Effects of betulin on extracellular signal-regulated kinases (ERK) signaling. K562S CML cells were untreated (K562S) or treated with 1% DMSO, 50 or 100μM of betulin or 20μM of imatinib mesylate for 6 hours and immunoblot analysis was conducted as described in the Methods section. Extracts of K562S cells were analyzed by SDS-PAGE followed by Western blotting with antibodies directed against phospho-ERK1/2 (Thr202/Tyr204) (a) and α-Tubulin (b).