

# Design, Synthesis, and Cancer Cell Growth Inhibitory Activity of Triphenylphosphonium Derivatives of the Triterpenoid Betulin

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## Abstract

© 2017 The American Chemical Society and American Society of Pharmacognosy. A series of new triphenylphosphonium (TPP) derivatives of the triterpenoid betulin (1, 3-lup-20(29)--ne-3 $\beta$ ,28-diol) have been synthesized and evaluated for cytotoxic effects against human breast cancer (MCF-7), prostate adenocarcinoma (PC-3), vinblastine-resistant human breast cancer (MCF-7/Vinb), and human skin fibroblast (HSF) cells. The TPP moiety was applied as a carrier group through the acyl linker at the 28- or 3- and 28-positions of betulin to promote cellular and mitochondrial accumulation of the resultant compounds. A structure-activity relationship study has revealed the essential role of the TPP group in the biological properties of the betulin derivatives produced. The present results showed that a conjugate of betulin with TPP (3) enhanced antiproliferative activity toward vinblastine-resistant MCF-7 cells, with an IC<sub>50</sub> value as low as 0.045  $\mu$ M.

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