



## Bromoacetoxycalcidiol: A Vitamin D Derivative with Antitumor Activity

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### Field

Primary Application:  
Biomedical Applications  
Drug Discovery

Secondary application(s):  
Cancer treatment

**Patent/Patent Application  
Number:**  
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Bromoacetoxycalcidiol (B3CD) is a derivative of 1,25-dihydroxy-vitamin D<sub>3</sub> (calcitriol) that does not cause hypercalcemia when administered in high doses but does induce apoptosis in several tumor cell lines in vitro and inhibits angiogenesis in a chick chorioallantoic membrane assay (CAM).

### Technology

Despite the existence of a number of drugs which have proven useful in treating cancer, there remains a need to find and use additional drugs which either have comparatively lower toxic side effects, can be used to overcome drug resistance, or act through new mechanisms. Analogs of vitamin D are of interest in this regard as vitamin D has been demonstrated to have a range of biological effects more like a hormone than a vitamin. A key challenge is finding analogs that do not induce the hypercalcemia that results from high doses of vitamin D itself.

Calcidiol is a precursor of calcitriol that is found in serum at concentrations approximately 1,000 fold higher than calcitriol, and which does not induce hypercalcemia. (It is thought that this difference in biological function is related to the 3-epi orientation of the hydroxyl group in calcidiol.) This led the inventor and his colleagues to synthesize a series of analogs of calcidiol, where the 3-hydroxyl group was replaced by several chemical groups including derivatives of bromine, other halogens, amines, azides, and others. In particular, the B3CD analog was tested in a number of in vitro and in vivo assays.

A key observation was that doses of B3CD up to 170 µg/kg body weight in mice showed no effect on body weight or serum calcium levels, suggesting that B3CD may not be toxic. B3CD did show antiproliferative effects and cytotoxic activity against a panel of tumor cell lines in vitro including neuroblastic, ovarian, and prostate cancer cells, and against normal endothelial cells. It was not cytotoxic or antiproliferative against breast, pancreatic, and osteosarcoma tumor cells nor against skin, smooth muscle, or macrophages. Further, B3CD was seen to inhibit vascular endothelial growth factor (VEGF) activity in a CAM assay. Other assays suggest that B3CD may be acting by inhibition of phosphorylation of ERK and AKT and by inhibition of TrkB signaling.

A pending patent application covering various derivatives of calcidiol and their uses in tumor treatment is published as WO/2006/096555.

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