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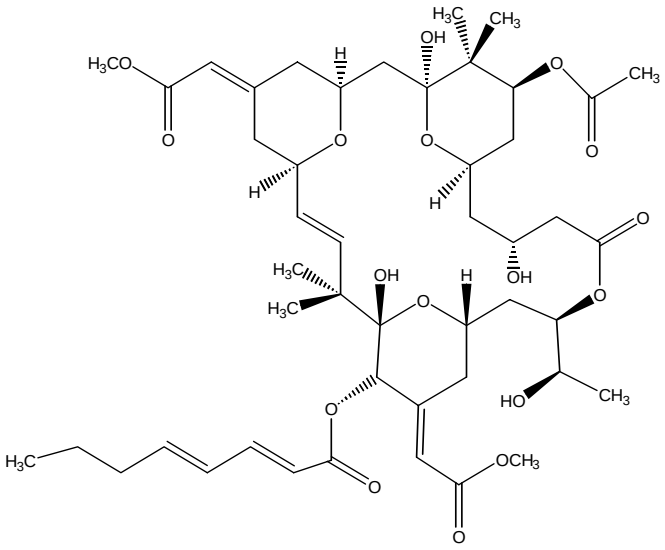
ProductInformation

Bryostatin 1

Product Number **B 7431**
Storage Temperature –20 °C

CAS# 83314-01-6



Product Description
Molecular Formula: $C_{47}H_{68}O_{17}$
Molecular Weight: 905.0
Supplied as white powder or colorless film
Purity: Approximately 99% by HPLC

Bryostatin 1 is a macrolactone isolated from the marine bryozoan, *Bugula neritina*, that modulates protein kinase C (PKC) activity. Bryostatins compete with the phorbol esters and diacylglycerols for binding to the cysteine-rich domains CRD1 and CRD2 of PKC. However, while the phorbol esters are tumor promotors, the bryostatins have antineoplastic activity. Bryostain 1 induces an initial rapid activation and autophosphorylation of PKC that results in the translocation of the PKC enzyme to the membrane. PKC is subsequently down-regulated by ubiquitination and proteolysis.[1]

The effects of bryostatin 1 are cell type and PKC isoform dependent. For example, in LNCaP human prostate cancer cells, bryostatin 1 induces a transient activation and membrane translocation of PKCα followed by down-regulation, while it induces a prolonged translocation of PKCδ and PKCε to non-nuclear membranes.[2] Other studies have also indicated that PKCδ is not down-regulated by bryostatin 1.[3]

Through its activation of PKC, bryostatin-1 induces the phosphorylation of other kinases and regulatory proteins. For example, in NB4 promyelocytic leukemia cells bryostatin 1 induces cell differentiation and the hyperphosphorylation of an abnormal p53 via the MAP kinase signaling pathway. Hyperphosphorylated p53 is subsequently ubiquitinated and degraded.[4]
Bryostatin 1 also induces the phosphorylation of the oncogene Bcl-2 by PKCα. In the acute lymphoblastic leukemia cell line, Reh, the phosphorylation of Bcl-2 leads to its ubiquitin-mediated degradation.[5] However, in mouse embryonic fibroblasts (MEF), the phosphorylation of Bcl-2 protects against heat-induced apoptosis.[6]

Bryostatin 1 sensitizes cancer cells to the cytotoxic effects of anti-cancer agents. For example, chronic preexposure of leukemia cell lines to bryostatin 1 down-regulates PKC and enhances the cytotoxicity of 1-β-D-arabinofuranosylcytosine (Ara-C).[7] In Reh cells bryostatin 1 enhances the the cytotoxicity of auristatin PE and vincristine, perhaps via the down-regulation of Bcl-2.[8]

Preparation Instructions
Bryostatin 1 is soluble in DMSO and ethanol.

Storage/Stability
Store tightly sealed at –20 °C. Bryostatin 1 binds to glass and plastic surfaces in aqueous solutions.

References

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4. Song, X.D., et al., Mitogen-activated protein kinase is involved in the degradation of p53 protein in the Bryostatin-1-induced differentiation of the acute promyelocytic leukemia NB4 cell line. J. Biol. Chem., **274,** 1677-1682 (1999).
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6. Bai, X.C., et al., Phospholipase $C_{\gamma 1}$ is required for survival in heat stress: involvement of protein kinase C-dependent Bcl-2 phosphorylation. J. Biochem., **131**, 207-212 (2002).
7. Jarvis, W.D., et al., Evidence for involvement of mitogen-activated protein kinase, rather than stress-activated protein kinase, in potentiation of 1-beta-D-arabinofuranosylcytosine-induced apoptosis by interruption of protein kinase C signaling. Mol. Pharmacol., **54,** 844-856 (1998).
8. Wall, N.R., et al., Modulation of cIAP-1 by novel antitubulin agents when combined with bryostatin 1 results in increased apoptosis in the human early pre-B acute lymphoblastic leukemia cell line Reh. Biochem. Biophys. Res. Commun., **9**, 76-80 (1999).

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