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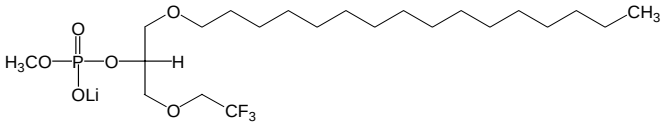
ProductInformation

MJ 33

Product Number **M 3315**
Storage Temperature 2-8 °C

CAS #: 199106-13-3
Synonyms: 1-Hexadecyl-3-(trifluoroethyl)-*sn*-glycero-2-phosphomethanol, lithium



Product Description
Molecular Formula: $C_{22}H_{43}F_3O_6PLi$
Molecular Weight: 498.5
Appearance: white solid
Purity: 90% by NMR

MJ 33 is an active site-directed specific inhibitor of Type I (pancreatic) and bee venom phospholipase A_2 (PLA_2). PLA_2 designates a class of enzymes with an approximate molecular weight of 14 kDa that hydrolyzes the *sn*-2 ester of glycerophospholipids to produce a fatty acid and a lysophospholipid. Based on amino acid sequences, the known PLA_2s can be divided into ten distinct groups with specific functions and tissue distribution. Since naturally-occurring phospholipids are membrane constituents that are essentially insoluble in water, in order to access the substrate PLA_2s must bind to the lipid-aqueous interface as functionally active monomers. Subsequently PLA_2 binds to the substrate molecule to form a complex that then becomes activated on an ionic interface.[1]

Many compounds have been identified that are nonselective inhibitors of PLA_2 isozymes and, thus, cannot be used to study the role of specific PLA_2 isozymes in complex cellular processes. Determination of crystal structures of the PLA_2 enzyme made it possible to identify anionic binding sites on PLA_2. Over 100 amphiphilic phosphoesters were tested for their ability to inhibit the active site of phospholipase A_2.[2] MJ 33 is a competitive, active site-directed inhibitor, that selectively complexes with Type 1B PLA_{2A} (bee venom, pancreatic, and acidic lung PLA_2). In crystallographic studies, MJ 33 and five sulfate or phosphate anions are bound between the two subunits of the PLA_2 dimer. The *sn*-2-phosphate of MJ 33 binds to the active site of the A subunit of PLA_{2A} and the alkyl chain extends into the active site slot of the B subunit across the subunit interface.[1]

MJ 33 at 3 mol% produced 95% inhibition of pancreatic PLA_2. Mol % is defined as ([MJ 33]/([MJ 33] + [PG]) ×100, where PG is the concentration of phosphatidyl-glycerol. Bee venom, pancreatic, and acidic lung PLA_2s share common characteristics. All are soluble enzymes that are active at acidic pH (4.5–5.0) and are calcium-independent. MJ 33 has poor affinity for the Type II human synovial PLA_2 and has only moderate affinity toward lysosomal PLA_2 isolated from macrophages (IC_{50} = 15 mol%).[3,4,5] Thus, MJ 33 is a valuable tool for determining the role of Type 1B PLA_2 in cellular processes.

Preparation Instructions
MJ 33 is soluble in water at 10 mg/ml with warming to 60 ºC.

Storage/Stability
Store at 2 to 8 ºC under nitrogen, in a desiccator and protected from light.

References
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2. Jain, M. K., et al., Active-site-directed specific competitive inhibitors of phospholipase A_2: novel transition-state analogues. Biochemistry, **30**, 10256–10268 (1991).
3. Fisher, A. B., Dodia, C., Lysosomal-type PLA_2 and turnover of alveolar DPPC. Am. J. Physiol. Lung Cell Mol. Physiol., **280,** L748-L754 (2001).

4. Akiba, S., et al., Characterization of acidic Ca^{2+}-independent phospholipase A_2 of bovine lung. .Comp. Biochem. Physiol. B. Biochem. Mol. Biol., **120**, 393-404 (1998).

5. Shinozaki, K., Waite, M., A novel phosphatidyl-glycerol-selective phospholipase A_2 from macrophages. Biochemistry., **38**, 1669-1675 (1999)

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