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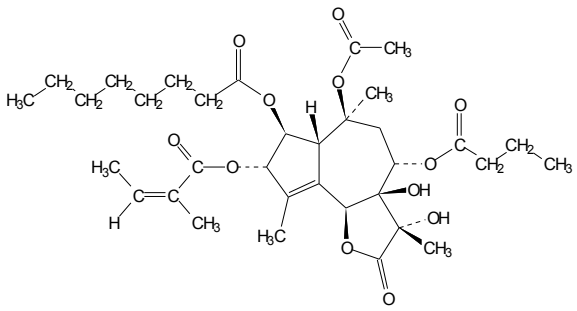
# Product Information

## Thapsigargin

Catalog Number **T9033**
Storage Temperature –20 °C

CAS RN: 67526-95-8
Synonyms: Octanoic acid derivative of azuleno [4,5-b]furan[1]

### Description
Appearance: Solid or clear film inside vial
Molecular formula: $C_{34}H_{50}O_{12}$
Molecular weight: 650.75



An HPLC method for the separation and determination of the main thapsigargins found in the plant has been reported.[3] The stereochemistry, $^{13}C$ NMR spectral data and the X-ray analysis for the epoxide derivative have been reported.[4,5]

### Precautions and Disclaimer
This product is for R&D use only, not for drug, household, or other uses. Please consult the Material Safety Data Sheet for information regarding hazards and safe handling practices.

### Method Of Preparation
Thapsigargin (TG) is extracted from the plant Thapsia garganica L. with methanol and purified by HPLC.[6] A method of isolation from the plant extract has been reported.[7]

### Storage/Stability
The product should be stable for at least one year when stored at –20 °C.[6]

### Solubility/Solution Stability:
TG is soluble in DMSO[8] and in ethanol[9]. No initial concentrations of TG were given for either solvent but it was noted that the final concentrations were: in DMSO, less than 1% (v/v)[8]; ethanol, did not exceed 1% of the total volume (working concentrations in ethanol were from 70-140 µM).[9] Neither amount of solvent had any adverse effects in the described systems. Preparation of a 3% (w/v) solution in deuterated DMSO was described.[4] TG has been solubilized in acetonitrile at 10 mg/ml producing a clear, colorless solution.[2] TG is also soluble in methanol, diethyl ether, and methylene chloride.[6] Solutions are recommended to be prepared fresh.[6] However, if necessary, solutions can be stored at –20 °C under argon or nitrogen.[6] A 1 mM solution in DMSO was reportedly stored at –20 °C (no storage time given).[10]

### Usage/Applications:
TG is an effective inhibitor of the $Ca^{2+}$ ion pump proteins of intracellular membranes located in sarcoplasmic reticulum (SR) and endoplasmic reticulum (ER) of skeletal, cardiac, muscle and brain microsomes.[9,11] A concentration of 100 nM was effective in inhibiting the SR $Ca^{2+}$-ATPase from cardiac and skeletal muscles. The action of TG is restricted to enzymes in the SR pump in intact cardiac myocytes.[12] TG interacts strongly with the SR of $Ca^{2+}$-transport ATPase to form a 1:1 stoichiometric complex. The proposed mechanism of inhibition of $Ca^{2+}$-ATPase activity including the inhibition of $Ca^{2+}$ ion binding and enzyme phosphorylation have been reported.[13,14,15] TG releases intracellular $Ca^{2+}$ in rat hepatocytes by specific inhibition of a microsomal (ER) isoform of $Ca^{2+}$-ATPase enzyme.[16] TG, a cell permeant agent, activates platelets (at 1 µM) and this is mediated by an increase in the cytoplasmic free calcium ion level probably through stimulation of the passive calcium transport through specific channels (as shown by protein phosphorylation).[8,17,18] TG is a potent activator of different cell types involved in the inflammatory process.[19,20] The compound has also been shown to promote second-stage carcinogenesis in mouse skin which does not involve direct activation of protein

kinase C (as TPA does*) this suggests that it is a non-TPA type tumor promoter.[21] The incubation of isolated rat adipocytes with 100 nM TG increases the intracellular cytosolic $Ca^{2+}$ ion content 2-3-fold. TG reduced the insulin-stimulated glucose transport by about 40%.[22] Protein synthesis in cells was inhibited up to 10 nM of TG.[23] TG, up to 300 nM, activates a non-selective univalent and bivalent SK&F 96365- and Gd3+- sensitive cation entry pathway in human neutrophils.[10] At 200 nM, TG increases the sodium-dependent phosphate uptake in HeLa cells by mobilization of intracellular calcium independent of protein kinase C.[24] Additional studies report that inositol triphosphate ($IP_3$) and TG discriminate ER stores of $Ca^{2+}$ ions in rat brain and that $Ca^{2+}$ ion influx in human T lymphocytes is induced independently of $IP_3$ by mobilization of intracellular $Ca^{2+}$ ion stores.[25,26] At 10 ng/ml, TG stimulates arachidonic acid metabolism in rat peritoneal macrophages by acting as a selective $Ca^{2+}$ ion mobilizer without activating protein kinase C.[27] TG mobilizes intracellular $Ca^{2+}$ by an $IP_3$-independent mechanism in parotid acinar cells at 2 μM.[28] TG at 1.7 μM has been shown to release $Ca^{2+}$ ions from an intracellular $IP_3$-sensitive $Ca^{2+}$ ion store, in a neuronal cell line by a mechanism independent of the hydrolysis of phosphoinositides and activation of protein kinase C.[29] Studies on the effect of TG on vascular contractility concluded that TG inhibits the ability of cAMP to stimulate $Ca^{2+}$ ion uptake into the store by blocking its $Ca^{2+}$ ion pump.[30]

**General Notes:**
TG is a tumor promoting plant sesquiterpene lactone extract with a unique biological activity as $Ca^{2+}$-ATPase inhibitors in animal cells.[9,11,12,15,16,18] It is a skin irritant, a platelet activating[17], inflammatory[19,20] and tumor promoting[21] agent. TG is toxic and a possible carcinogen.

**References**

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*TPA, Phorbol 12-Myristate 13-Acetate

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