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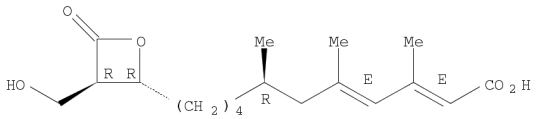
Product Information

Hymeglusin
from *Fusarium sp*.

Catalog Number **SML0301**
Storage Temperature –20 °C

CAS RN 29066-42-0
Synonyms: Antibiotic 1233A, F-244, L-659,699

Product Description



Molecular formula: $C_{18}H_{28}O_5$
Molecular weight: 324.41

Hymeglusin (1233A; F244; L-659-699) is a specific β-lactone inhibitor of eukaryotic hydroxymethylglutaryl-CoA synthase (HMGCS), a key enzyme in the cholesterol biosynthetic pathway.[1,2] Unlike other fungal metabolites, hymeglusin inhibits mevalonate biosynthesis by acting on HMG-CoA synthase, while other metabolites, such as lovastatin (mevinolin) and compactin, act as specific competitive inhibitors of the HMG-CoA reductase.[3] Inhibition results from covalent modification of the active Cys^{129} residue by the formation of a thioester adduct in the active site.[4,5] Hymeglusin show no inhibitory effect against fatty acid synthetase purified from *Sacharomyces serevisiae*.[3]

Hymeglusin was found to block the growth of *Enterococcus faecalis*. After removal of the inhibitor from the culture medium, a growth curve inflection point is observed. Upon hymeglusin inactivation, enzyme activity is restored at a rate that is 8-fold faster for human HMGCS than for the bacterial enzyme (mvaS). Structural studies explain these differences.[4]

Hymeglusin was also found to inhibit the replication of the dengue live virus (DEN-2 NGC virus) in K562 cells. Lovastatin inhibits DEN-2 NGC live virus replication in human peripheral blood mononuclear cells.[6]

Purity: ≥98% (HPLC)

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.

Preparation Instructions

Hymeglusin is soluble in DMSO, acetone, ethyl acetate and chloroform. The product is insoluble in water.

Storage/Stability

Store the product sealed at –20 °C. Under these conditions the product is stable for at least 3 years. A DMSO solution (1 mg/mL) is stable for one month at –20 °C.

References

1. Tomoda, H. et al., F-244 (A1233), a specific inhibitor of 3-hydroxy-3-methylglutaryl coenzyme A synthease: Taxonomy of producing strain, fermentation, isolation and biological properties. J. Antibiot., **XLI**, 247-249 (1987).
2. Wattanasin, S. et al., Enantiomeric synthesis of the beta-lactone precursor of the HMG-CoA synthase inhibitor (+)-F-(244). J. Org. Chem., **58**, 1610-1612 (1993).
3. Tomoda, H. et al., F-244 specifically inhibits 3-hydroxy-3-methylglutaryl coenzyme A synthase. Biochimia Biophysica Acta, **922**, 351-356 (1987).
4. Skaff, D.A. et al., The Biochemical and Structural Basis for Inhibition of *Enterococcus faecalis* HMG-CoA Synthase, mvaS, by Hymeglusin. Biochemistry, Epub ahead of print (2012).
5. Tomoda, H. et al., Binding site for fungal beta-lactone hymeglusin on cytosolic 3-hydroxy-3-methylglutaryl coenzyme A synthase. Biochim. Biophys. Acta, **1636**, 22-28 (2004).
6. Rothwell, C. et al., Cholesterol biosynthesis modulation regulates dengue viral replication. Virology, **389**, 8-19 (2009).

DWF,KAA,MAM 06/12-1