

3050 Spruce Street Saint Louis, Missouri 63103 USA Telephone 800-325-5832 • (314) 771-5765 Fax (314) 286-7828 email: techserv@sial.com sigma-aldrich.com

ProductInformation

MEVASTATIN Product Number M2537 Storage Temperature 2-8°C

CAS #: 73573-88-3 Synonyms: compactin, (+)-compactin, antibiotic ML 236B, ML 236B

Product Description



Appearance: white powder Molecular Formula: C₂₃H₃₄O₅ Formula Weight: 390.5 For Specifications, see Catalog

Mevastatin, an antibiotic, is a potent competitive inhibitor of hydroxymethylglutaryl-CoA reductase, the rate-limiting enzyme in cholesterol biosynthesis.^{1,2}

Mevastatin has been shown to cause apoptosis of myeloma cells, macrophages and osteoclasts. It appears that this is due to mevastatin's inhibition of post-translational prenylation of proteins such as Ras.³⁻⁶ Prenylation of Ras is required for its proper membrane binding and targeting.⁷ Similarly, a Ras-like GTPase, Rho, negatively regulates eNOS (endothelial nitric oxide synthase) expression, but mevastatin (1 – 10 μ M) increases eNOS mRNA and protein levels. It does this by blocking Rho geranylgeranylation which is necessary for Rho's membrane-associated activity.⁸

Mevastatin also inhibits myoblast fusion.⁹⁻¹¹ Myoblasts must fuse in order to form multinucleated myotubes. These myotubes go on to develop into muscle fibers. Fusion is accompanied by biochemical differentiation characterized by an increase in the expression of a number of different enzymes, in particular creatine phosphokinase. Mevastatin at concentrations as low as $0.25 \ \mu M$ reduced the creatine phosphokinase activity of myoblast cells, reduced the number of N-linked cell surface glycoproteins, and inhibited the incorporation of mannose from GDP-mannose into lipid-sugar and N-linked glycoprotein.¹¹ The conclusion is that mevastatin inhibits myoblast fusion by affecting the synthesis of intermediates needed for the production of the fusogenic cell surface N-linked glycoproteins. It should be noted that the fusion of the myoblasts is restored when the mevastatin is removed.¹

Precautions and Disclaimer

Please consult the Material Safety Data Sheet for handling recommendations before working with this material.

Preparation Instructions

Mevastatin is soluble in ethanol at 25 mg/mL and in DMSO at 25 mg/mL.

Storage/Stability

Store the powder at 2-8°C.

References

- 1. Endo, A. et al., FEBS Lett., 72, 323 (1976).
- Brown, M.S. et al., J. Biol. Chem., 253, 1121 (1978).
- 3. Luckman, S.P. et al., J. Bone Miner Res., 13, 581 (1998).
- 4. Coxon, F.P. et al., Mol. Pharmacol., 54, 631 (1998).
- 5. Shipman, C.M. et al., Cancer Res., 58, 5294 (1998).
- 6. Qui, M.S. et al., J. Cell Biol., 115, 795 (1991).

- 7. Seabra, M.C., Cell Signal, 10, 167 (1998).
- Laufs, U. and Liao, J.K., J. Biol. Chem., 273, 24266 (1998).
- 9. Cornell, R.B. et al., J. Cell Biol., 86, 820 (1980).
- 10. Jamieson, J.C. et al., Biochem. Cell Biol., 70, 408 (1992).
- 11. Belo, R.S. et al., Mol. Cell Biochem., 126, 159 (1993).

alc 02/10/99

Sigma brand products are sold through Sigma-Aldrich, Inc.

Sigma-Aldrich, Inc. warrants that its products conform to the information contained in this and other Sigma-Aldrich publications. Purchaser must determine the suitability of the product(s) for their particular use. Additional terms and conditions may apply. Please see reverse side of the invoice or packing slip.