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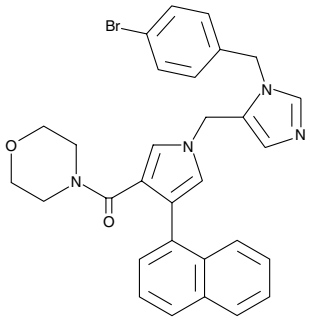
Product Information

LB 42708

Item No. 16428

CAS Registry No.: 226929-39-1
Formal Name: [1-[[1-[(4-bromophenyl)methyl]-1H-imidazol-5-yl]methyl]-4-(1-naphthalenyl)-1H-pyrrol-3-yl]-4-morpholinyl-methanone
MF: $C_{30}H_{27}BrN_4O_2$
FW: 555.5
Purity: ≥98%
Stability: ≥2 years at -20°C
Supplied as: A crystalline solid
UV/Vis.: λ_{max}: 223, 296 nm



Laboratory Procedures

For long term storage, we suggest that LB 42708 be stored as supplied at -20°C. It should be stable for at least two years.

LB 42708 is supplied as a crystalline solid. A stock solution may be made by dissolving the LB 42708 in the solvent of choice. LB 42708 is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, which should be purged with an inert gas. The solubility of LB 42708 in these solvents is approximately 30 mg/ml.

LB 42708 is sparingly soluble in aqueous buffers. For maximum solubility in aqueous buffers, LB 42708 should first be dissolved in ethanol and then diluted with the aqueous buffer of choice. LB 42708 has a solubility of approximately 0.1 mg/ml in a 1:5 solution of ethanol:PBS (pH 7.2) using this method. We do not recommend storing the aqueous solution for more than one day.

Farnesylation, the post-translational addition of a 15-carbon isoprenyl group, alters the function of several proteins, including Ras proteins.[1,2] LB 42708 is a potent inhibitor of farnesyltransferase (FTase), blocking farnesylation of HRas, NRas, and KRas4B with IC_{50} values of 0.8, 1.2, and 2.0 nM, respectively.[3] It displays over 50,000-fold selectivity for FTase over geranylgeranyltransferase I.[3] LB 42708 prevents the farnesylation of HRas in response to LPS plus IFN-γ (IC_{50} = 10 nM), preventing activation of NF-κB as well as downstream signaling.[3] These effects are obtained both in RAW 264.7 mouse macrophages and in mice.[3] LB42708 also inhibits Ras-dependent signaling in endothelial cells, stopping VEGF-mediated angiogenesis both *in vitro* and *in vivo*.[4]

References

1. Appels, N.M.G.M., Beijnen, J.H., and Schellens, J.H.M. Development of farnesyl transferase inhibitors: A review. *Oncologist* **10**, 565-578 (2005).
2. Berndt, N., Hamilton, A.D., and Sebti, S.M. Targeting protein prenylation for cancer therapy. *Nat. Rev. Cancer* **11(11)**, 775-791 (2011).
3. Na, H.-J., Lee, S.-J., Kang, Y.-C., *et al.* Inhibition of farnesyltransferase prevents collagen-induced arthritis by down-regulation of inflammatory gene expression through suppression of $p21^{ras}$-dependent NF-κB activation. *J. Immunol.* **173(2)**, 1276-1283 (2004).
4. Kim, C.-K., Choi, Y.K., Ha, K.-S., *et al.* The farnesyltransferase inhibitor LB42708 suppresses vascular endothelial growth factor-induced angiogenesis by inhibiting Ras-dependent mitogen-activated protein kinase and phosphatidylinositol 3-kinase/Akt signal pathways. *Mol. Pharmacol.* **78(1)**, 142-150 (2010).

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