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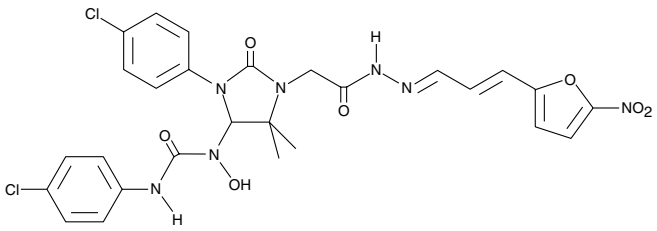
Product Information

Eeyarestatin 1

Item No. 10012609

CAS Registry No.: 412960-54-4
Formal Name: 3-(4-chlorophenyl)-4-[[[(4-chlorophenyl) amino]carbonyl] hydroxyamino]-5,5-dimethyl-2-oxo-1- imidazolidineacetic acid 2-[3-(5-nitro-2-furanyl)-2-propen-1-ylidene]hydrazide
MF: $C_{27}H_{25}Cl_2N_7O_7$
FW: 630.4
Purity: ≥98%
Stability: ≥2 years at -20°C
Supplied as: A crystalline solid
UV/Vis.: λ_{max}: 245, 285, 380 nm



Laboratory Procedures

For long term storage, we suggest that eeyarestatin 1 be stored as supplied at -20°C. It should be stable for at least two years.

Eeyarestatin 1 is supplied as a crystalline solid. A stock solution may be made by dissolving the eeyarestatin 1 in the solvent of choice. Eeyarestatin 1 is soluble in organic solvents such as DMSO and dimethyl formamide, which should be purged with an inert gas. The solubility of eeyarestatin 1 in these solvents is approximately 30 mg/ml.

Eeyarestatin 1 is sparingly soluble in aqueous solutions. To enhance aqueous solubility, dilute the organic solvent solution into aqueous buffers or isotonic saline. If performing biological experiments, ensure the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. We do not recommend storing the aqueous solution for more than one day.

Terminally misfolded proteins, recognized by chaperones on the endoplasmic reticulum (ER), are transported to depots for ubiquitination and proteasomal degradation by the ER-associated protein degradation (ERAD) pathway. Eeyarestatin 1 is an inhibitor of the ERAD pathway, blocking the degradation of misfolded proteins at a dose of 8 µM.[1] It associates with the p97-associated deubiquitinating complex in cells, preventing deubiquitination of substrates by ataxin-3.[2,3] Eeyarestatin 1, at 4 µM, interferes with both retrograde and anterograde trafficking of proteins, including certain toxins, and potentially, viruses.[4]

References

1. Fiebiger, E., Hirsch, C., Vyas, J.M., *et al.* Dissection of the dislocation pathway for type I membrane proteins with a new small molecule inhibitor, eeyarestatin. *Mol. Biol. Cell* **15**, 1635-1646 (2004).
2. Wang, Q., Li, L., and Ye, Y. Inhibition of p97-dependent protein degradation by Eeyarestatin I. *J. Biol. Chem.* **283(12)**, 7445-7454 (2008).
3. Wang, Q., Shinkre, B.A., Lee, J.-G., *et al.* The ERAD inhibitor Eeyarestatin I is a bifunctional compound with a membrane-binding domain and a p97/VCP inhibitory group. *PLoS One* **5(11)**, 1-12 (2010).
4. Aletrari, M.O., McKibbin, C., Williams, H., *et al.* Eeyarestatin 1 interferes with both retrograde and anterograde intracellular trafficking pathways. *PLoS One* **6(7)**, 1-11 (2011).

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