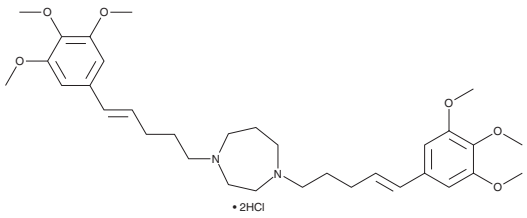
PRODUCT INFORMATION

K-7174 (hydrochloride)

Item No. 32773

CAS Registry No.:	191089-60-8
Formal Name:	hexahydro-1,4-*bis*[(4E)-5-(3,4,5-trimethoxyphenyl)-4-penten-1-yl]-1H-1,4-diazepine, dihydrochloride
MF:	$C_{33}H_{48}N_2O_6 \bullet 2HCl$
FW:	641.7
Purity:	≥98%
UV/Vis.:	λ_{max}: 222, 268 nm
Supplied as:	A crystalline solid
Storage:	-20°C
Stability:	≥4 years



Information represents the product specifications. Batch specific analytical results are provided on each certificate of analysis.

Laboratory Procedures

K-7174 (hydrochloride) is supplied as a crystalline solid. A stock solution may be made by dissolving the K-7174 (hydrochloride) in the solvent of choice, which should be purged with an inert gas. K-7174 (hydrochloride) is soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide. The solubility of K-7174 (hydrochloride) in these solvents is approximately 5, 10, and 30 mg/ml, respectively.

Further dilutions of the stock solution into aqueous buffers or isotonic saline should be made prior to performing biological experiments. Ensure that the residual amount of organic solvent is insignificant, since organic solvents may have physiological effects at low concentrations. Organic solvent-free aqueous solutions of K-7174 (hydrochloride) can be prepared by directly dissolving the crystalline solid in aqueous buffers. The solubility of K-7174 (hydrochloride) in PBS, pH 7.2, is approximately 1 mg/ml. We do not recommend storing the aqueous solution for more than one day.

Description

K-7174 is a 20S proteasome inhibitor.[1] It inhibits the β1, β2, and β5 catalytic subunits of the 20S proteasome when used at a concentration of 5 µM. K-7174 (10 µM) reduces TNF-α- or IL-1β-induced adherence of U937 monocytes to human umbilical vein endothelial cells (HUVECs) in a co-culture model of monocyte-endothelial cell adhesion.[2] It inhibits tumor growth in U266 and RPMI-8226 multiple myeloma mouse xenograft models when administered at a dose of 75 mg/kg.[3] K-7174 also inhibits the GATA consensus sequence, reducing TNF-α-induced binding of HUVEC nuclear extracts to GATA motifs in the *VCAM1* promoter in an EMSA when used at a concentration of 30 µM.[2,4]

References

1. Kikuchi, J., Shibayama, N., Yamada, S., *et al.* Homopiperazine derivatives as a novel class of proteasome inhibitors with a unique mode of proteasome binding. *PLoS One* **8(4)**, e60649 (2013).
2. Umetani, M., Nakao, H., Doi, T., *et al.* A novel cell adhesion inhibitor, K-7174, reduces the endothelial VCAM-1 induction by inflammatory cytokines, acting through the regulation of GATA. *Biochem. Biophys. Res. Commun.* **272(2)**, 370-374 (2000).
3. Kikuchi, J., Yamada, S., Koyama, D., *et al.* The novel orally active proteasome inhibitor K-7174 exerts anti-myeloma activity *in vitro* and *in vivo* by down-regulating the expression of class I histone deacetylases. *J. Biol. Chem.* **288(35)**, 25593-25602 (2013).
4. Imagawa, S., Nakano, Y., Obara, N., *et al.* A GATA-specific inhibitor (K-7174) rescues anemia induced by IL-1β, TNF-α, or L-NMMA. *FASEB J.* **17(12)**, 1742-1744 (2003).

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