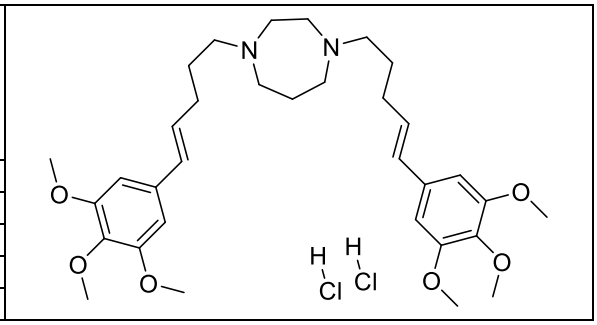
Product data sheet

MedKoo Cat#: 406454 Name: K-7174-2HCl CAS#: 191089-60-8 (HCl) Chemical Formula: $C_{33}H_{50}Cl_2N_2O_6$ Molecular Weight: 640.3	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

K-7174 is a novel orally active, potent proteasome inhibitor. K-7174 exerts anti-myeloma activity in vitro and in vivo by down-regulating the expression of class I histone deacetylases. K-7174 kills bortezomib-resistant myeloma cells carrying a β5-subunit mutation in vivo and primary cells from a patient resistant to bortezomib. K-7174 is also a GATA-specific inhibitor, which may have potential application in treating anemia of chronic disease.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
Water	15	23.38

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.56 mL	7.81 mL	15.62 mL
5 mM	0.31 mL	1.56 mL	3.12 mL
10 mM	0.16 mL	0.78 mL	1.56 mL
50 mM	0.03 mL	0.16 mL	0.31 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. Kikuchi J, Yamada S, Koyama D, Wada T, Nobuyoshi M, Izumi T, Akutsu M, Kano Y, Furukawa Y. 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. 2013 Aug 30;288(35):25593-25602. doi: 10.1074/jbc.M113.480574. Epub 2013 Jul 22. PMID: 23878197; PMCID: PMC3757220.

2. Imagawa S, Nakano Y, Obara N, Suzuki N, Doi T, Kodama T, Nagasawa T, Yamamoto M. A GATA-specific inhibitor (K-7174) rescues anemia induced by IL-1beta, TNF-alpha, or L-NMMA. FASEB J. 2003 Sep;17(12):1742-4. doi: 10.1096/fj.02-1134fje. Epub 2003 Jul 18. PMID: 12958195.

In vivo study

1. Kikuchi J, Yamada S, Koyama D, Wada T, Nobuyoshi M, Izumi T, Akutsu M, Kano Y, Furukawa Y. 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. 2013 Aug 30;288(35):25593-25602. doi: 10.1074/jbc.M113.480574. Epub 2013 Jul 22. PMID: 23878197; PMCID: PMC3757220.

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2. Imagawa S, Nakano Y, Obara N, Suzuki N, Doi T, Kodama T, Nagasawa T, Yamamoto M. A GATA-specific inhibitor (K-7174) rescues anemia induced by IL-1beta, TNF-alpha, or L-NMMA. FASEB J. 2003 Sep;17(12):1742-4. doi: 10.1096/fj.02-1134fje. Epub 2003 Jul 18. PMID: 12958195.

7. Bioactivity

Biological target:

K-7174 dihydrochloride is a novel cell adhesion inhibitor; inhibits the expression of vascular cell adhesion molecule-1 (VCAM-1) induced by either IL-1β or TNF-α.

In vitro activity

First, we examined the cytotoxic effect of K-7174 on MM cell lines using MTT assays. K-7174 significantly inhibited the growth of three MM cell lines in a dose-dependent manner (Fig. 1B). Next, we confirmed the anti-myeloma activity of K-7174 using primary MM cells. CD138-positive cells isolated from bone marrow samples of 6 patients were cultured in the absence or presence of K-7174 for 2 days, followed by annexin-V staining to assess the induction of apoptosis. K-7174 significantly increased the percentage of annexin-V-positive cells in all cases examined (Fig. 1C).

Reference: J Biol Chem. 2013 Aug 30;288(35):25593-25602. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23878197/

In vivo activity

The in vivo efficacy was examined using a xenograft mouse model. Either RPMI8226 or U266 cells were inoculated subcutaneously into NOD/SCID mice in the right thigh at 3 × 107 or 1 × 107 cells. When measurable tumors developed (usually after 4 days), either K-7174 (75 mg/kg) or vehicle (3% DMSO in 0.9% NaCl) was intraperitoneally administered once daily for 14 days (n = 3–4 in each group). The tumor volume between vehicle-control and K-7174-treated groups were compared on day 14. The tumor volume was significantly lower in the K-7174-treated group than in the vehicle-control group (Fig. 2, A and B). However, the K-7174-treated group had a significant body weight reduction after 10 days (data not shown). Therefore, the same set of experiments was repeated with reduced doses (30 and 50 mg/kg). Although no body weight reduction was observed, K-7174 failed to inhibit tumor growth at these doses (data not shown). To test the effects of oral administration, either K-7174 (50 mg/kg) or vehicle (3% DMSO in 0.9% NaCl) was orally administered once daily for 14 days (n = 3–4 in each group). The dose of K-7174 was determined to be well tolerated by mice without obvious side effects including weight loss in pilot experiments (data not shown). The tumor volume was compared between vehicle-control and K-7174-treated groups for up to 28 days. As a result, tumor volume was significantly lower in the K-7174-treated group than in the vehicle-control group (Fig. 2, C and D). There were no obvious side effects including body weight reduction, leukocytopenia, thrombocytopenia, anemia and hepatic dysfunction in both vehicle-control and K-7174-treated groups (the data on day 21 are shown in Table 1). To examine the proteasome inhibitory effect of K-7174 in vivo, the accumulation of ubiquitinated proteins was determined in inoculated tumors after oral administration of K-7174. As expected, a 2–4-fold accumulation of ubiquitinated proteins was observed in tumor cells in the K-7174-treated group but not in the vehicle-control group (Fig. 2E). This suggests that K-7174 could effectively inhibit proteasome activity in vivo. Taken together, these data demonstrate the potent anti-myeloma activity of K-7174 in vivo and more importantly, that oral administration is more effective than intraperitoneal injection.

Reference: J Biol Chem. 2013 Aug 30;288(35):25593-25602. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23878197/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.