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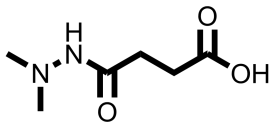
KDM2/7 Histone Demethylases Inhibitor – Daminozide

Chemical Name: N-(dimethylamino)succinamic acid



Molecular Weight:	160.17
Formula:	$C_6H_{12}N_2O_3$
Purity:	≥98%
CAS#:	1596-84-5
Solubility:	DMSO up to 100 mM
Storage	Powder: 4°C 1 year DMSO: 4°C 3 month -20°C 1 year

Biological Activity:

Daminozide is a potent and selective small molecule inhibitor of the KDM2/7 family of human JmjC histone demethylases. It inhibits KDM2A at IC_{50} ~1.5 μM, PHF8 at IC_{50} ~0.55 μM, and KIAA1718 at IC50 ~2.1 μM. It has at least 60-fold selectivity as an inhibitor of the KDM2/7 subfamily over the other demethylase subfamily members such as KDM3A, KDM4E, KDM5C and KDM6B, and exhibits no inhibition even at 1 mM for PHD2, FIH, and BBOX1 (all of which are important 2OG oxygenases). The X-ray co-crystal structures revealed the daminozide's inhibition mode: it binds in the 2OG binding pocket and chelates to the active site metal via its acylhydrazide carbonyl and dimethylamino groups. The selectivity of daminozide for the KDM2/7 subfamily could, at least in part, arise from a "snug fit" obtained via binding in the position trans to His247 wherein its two methyl groups are accommodated in a tight hydrophobic pocket (formed by Val255, Ile313, and Tyr257), which is conserved in the KDM2/7subfamily. Given the link between JmjC enzymes and diseases (such as cancer, metabolic disease, neurological disease, and inflammation), further studies on the biological effects of daminozide is of great interest.

How to Use:

In vitro: Daminozide was used at 10-20 μM final concentration in vitro and in cellular assays.

In vivo: n/a

Reference:

1. Rose NR, et al. Plant Growth Regulator Daminozide Is a Selective Inhibitor of Human KDM2/7 Histone Demethylases (2012) J Med Chem. 55(14):6639-43.